# Developing and Evaluating a Collaborative Care Intervention for Depression

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## Declaration

I, Stephen Pilling, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

## Abstract

This thesis is concerned with the development and evaluation of the collaborative care model for the treatment of depression in primary care in the National Health Service (NHS). It begins with an outline of the problems experienced by people with depression and the challenge that their effective care presents to the healthcare system. It then considers the response of evidence-based medicine to this challenge and briefly reviews the commonly used tools of evidence-based medicine (such as systematic reviews and clinical guidelines). The origins of the collaborative care model in the treatment of chronic physical health problems are then reviewed to provide a context for a subsequent review of the current evidence for collaborative care for depression. Following this review the main elements of the effective treatment of depression are examined and include systematic reviews of the major psychological and pharmacological treatments. The competences required to deliver low-intensity brief psychological interventions are also developed and described. The design, implementation and evaluation of an exploratory trial of collaborative care of depression are then described and set in an overall framework for the evaluation of complex interventions as outlined by the Medical Research Council. The outcomes of the trial and a parallel process evaluation are then presented and the limitations of the trial considered. The implications of the trial for the future development and evaluation of collaborative care in the NHS are discussed.

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# 1. Depression: A Challenge for Evidence-Based Medicine

## 1.1 Introduction

Depression is the most common psychiatric disorder, potentially affecting everyone: men and women, the old and the young (Kessler *et al.*, 2003). In primary care settings rates of depression of up to 10% have been reported (Katzelnick *et al.*, 2000), and in the UK it has been estimated that up to one in four women and one in ten men suffer at least one episode of depression requiring treatment during their lifetimes (National Depression Campaign, 1999). More recently, Andrews and colleagues (2005), using data drawn from a modelling study and two prospective studies of the prevalence of depression (focusing on children and adolescents and older people respectively), have suggested that the previous estimates of a lifetime risk of depression of around 10% may be an underestimate; they go on to suggest that a remarkably high lifetime risk of approaching 50% may be more accurate. However, data from a recent large-scale, well-conducted epidemiological study in the US by Kessler and colleagues (2003), who report a lifetime prevalence of 16.2% and a 12-month prevalence of 6.6%, would suggest considerable caution before adopting the estimates of Andrews and colleagues (2005).

Depression is characterised by an absence of positive affect (loss of interest and enjoyment in everyday life), low mood and a range of associated emotional, cognitive, physical and behavioural symptoms. Distinguishing depression from 'normal' low mood can be difficult, but diagnosis is based on an assessment of the persistence and severity of the depressive symptoms along with the presence of other symptoms and the degree of functional and social impairment. Typically, mood in depression is unreactive to circumstance, remaining low throughout the course of each day, although for some people mood varies diurnally with gradual improvement throughout the day. Behavioural and physical symptoms include tearfulness, irritability, social withdrawal, reduced sleep, reduced appetite (which can to significant weight loss), lack of libido, fatigue and diminished activity, although agitation is also common as is increased anxiety. Along with a loss of interest and enjoyment in everyday life, feelings of guilt

and worthlessness are common, as is low self-esteem, loss of confidence, feelings of helplessness, suicidal ideation and attempts at self-harm or suicide. Cognitive changes in depression include poor concentration and reduced attention, recurrent negative thoughts, mental slowing and rumination (Cassano & Fava, 2002). Depression is often comorbid with anxiety, with epidemiological studies reporting the comorbidity of depression with anxiety disorders in the region of 50% (Melartin *et al.*, 2002) but also with a range of other disorders including personality disorder (Brown *et al.*, 2001).

Formal diagnosis of depression in the *International Classification of Diseases* – 10 (ICD-10; World Health Organization, 1992) is based on a list of 10 symptoms, and classifies the disorder as follows: mild depression (4 symptoms, which must include one of the following: persistent sadness or low mood; and loss of interests or pleasure or fatigue or low energy); moderate depression (5-6 symptoms); and severe depression (7 symptoms or more, with or without various psychotic symptoms)[1]. Symptoms must be present for at least 2 weeks. Although it is doubtful whether the severity of depression can be adequately captured in a simple symptom count, there is evidence of increasing personal and functional impairment as the symptom count increases (Faravelli *et al.*, 1996). Nevertheless, when arriving at a diagnosis of depression consideration should also be given to the degree of impairment in social and personal functioning as well as personal history.

Depression has a negative impact on an individual's quality of life and daily functioning and also on wider society, with increased demands on healthcare resources and lost productivity (Katzelnick *et al.*, 2000). For example, Kessler and colleagues (2003) using the Sheehan Disability Scale (Leon *et al.*, 1997), reported that 59.3% of their sample who had been depressed in the previous 12 months had severe or very severe role impairment. It is therefore not surprising that depression is currently the fourth leading cause of burden among all diseases and is projected to be the highest ranking cause of burden of disease in developed countries by the year 2020 (World Health Organization, 2001).

[1] The other commonly used diagnostic system, DSM-IV (American Psychiatric Association, 1994), requires 5 symptoms for a diagnosis of depression to be made. The ICD-10 system is described here as it is the system used in the UK and formed the basis for the diagnostic advice to the GPs in the trial conducted for this thesis.

The average age of onset of depression is the mid 20s, although a substantial proportion of people with depression have their first depressive episode in childhood or adolescence (Fava & Kendler, 2000). Early-onset depression (at or before 20 years of age) is associated with a significantly increased vulnerability to relapse (Giles *et al.*, 1989). For many people depression is a chronic disorder. An international study from 14 centres demonstrated that 50% of people identified with a mental disorder in the initial phase of the study still met diagnostic criteria for depression 1 year later (Goldberg *et al.*, 1998).This finding is confirmed by a number of studies, which also show that at least 50% of people will go on to have at least one further episode of major depression following their first; following a second or third episode, the risk of further relapse rises to 70% and 90% respectively (Kupfer, 1991).

The prevalence of depression is also significantly affected by a range of socio-demographic factors including gender, age, marital status, social class, education and employment (Meltzer *et al.*, 1995a & b). For example, the estimated point prevalence for depression among 16 to 65 year olds differs between females (25/1000) and males (17/1000), although the over-representation of females in this age group is reversed after the age of 55 (Meltzer *et al.*, 1995a & b). Higher prevalence of depression is associated with being separated from a partner (56/1000 female, 111/1000 male), being widowed for males (70/1000) and being divorced for females (46/1000). Lower prevalence of depression is associated with being married (17/1000 males; 14/1000 females). Single parents also have higher rates than couples, while couples with children have higher rates than those without (Meltzer *et al.*, 1995 a & b). Meltzer and colleagues (1995a) also identified differences in ethnic groups, although these differences seemed largely confined to women, with few if any differences in prevalence rates for males from any ethnic group. However, for females, rates varied considerably between ethnic groups, with the highest being found amongst Asians (51/1000), then whites (24/1000), and the lowest rates for West Indians or Africans (6/1000). Socio-economic factors and gender also appear to interact in a significant way. For example, the prevalence rates for unemployed women are over twice that of unemployed men (56/1000 versus 27/1000), whereas the rates are low for both sexes in full-time employment (11/1000 women vs 12/1000 men). Lower social class is associated with higher rates of depression, whereas completion of higher education

seems to have a protective function against its development, although this effect is more marked for men than it is for women (Meltzer *et al.*, 1995a & b). Rates for homeless people are very high, with a prevalence of 270/1000 for all types of depression (Meltzer *et al.*, 1995b). The magnitude of the impact of social factors can be discerned from a study in general practice by Ostler and colleagues (2001), which reported that almost 50% of the variance in the different rates of presentation of depression (range: 2.4% to 13.7%, depending upon the practice) could be accounted for by the level of neighbourhood social deprivation. Taken together, these data support the view that the prevalence of depression varies considerably with gender and a broad range of social and economic factors.

In addition to the social and occupational burdens imposed by depression, the disorder also has a significant impact on general physical morbidity and mortality. For example, death rates are significantly greater for those who are depressed following a myocardial infarction, not only in the immediate post-infarct period, but also for at least the following year (Lesperance & Frasure-Smith, 2000). In a range of other physical illnesses, evidence also suggests an increased mortality rate when comorbid depression is present (Cassano & Fava, 2002). Depression is also the leading cause of suicide, which accounts for just less than 1% of all deaths, of which nearly two-thirds occur in people with depression (Sartorius, 2001). There is often a negative impact on marital and family relationships, and if a parent is depressed, this may have a detrimental effect on a child's development (Ramchandani & Stein, 2003).

Effective pharmacological, psychological and psychosocial treatments exist for depression (for example, Goldberg *et al.*, 2004), but a number of factors may limit access to such treatments. First, many people with depression do not seek help. Meltzer and colleagues (2000) identified the following reasons for not seeking help: not believing that any help can be provided (28%); thinking that one should be able to cope with the problem oneself (28%); believing that it is not necessary to contact a doctor (17%); thinking that that the problem will get better by itself (15%); being too embarrassed to discuss it with anyone (13%); and being afraid of the consequences of the treatment, for example, admission to hospital (10%). Secondly, the problem of non-recognition of depression by healthcare professionals, even when a person presents with

problems in a healthcare setting, is considerable. Although the annual rate of depression in primary care can exceed 10%, studies indicate that GPs only recognise about 30% of cases (Goldberg, 1995). A major reason for this is that many people with depression consult for physical complaints and do not consider themselves to have any psychological problems, despite the presence of depressive symptoms (Katona and Livingston, 2000). Thirdly, for identified patients there may be limited treatment options available (for example, there may be a difficulty in accessing psychological treatments (Lovell & Richards, 2000)), or those that are available may be judged not to be acceptable (for example, although patients may be offered antidepressant medication, a significant proportion decline the offer, fail to obtain the antidepressants from the pharmacist or do not complete the treatment as prescribed (Hansen *et al.*, 2004)). Finally, the stigma associated with mental health problems generally (Sartorius, 2002) may account for the reluctance of depressed people to seek help.

The consequences of the problems described above can be seen by reference to the study by Kessler and colleagues (2003) where only 51.6% of those depressed in the previous year had been offered treatment and this treatment was rated as adequate in only 41.9% of cases. This confirms the picture from previous studies, which also report treatment often falling short of recommended practice (Katon *et al.*, 1992; Donoghue & Tylee, 1996; Young *et al.*, 2001), and therefore resulting in outcomes that are correspondingly below what is possible (Rost *et al.*, 1995).

### 1.2 The response of evidence-based medicine

The significant burden experienced by people with depression, the difficulties in its recognition in routine clinical care, the suboptimal treatment provided and the poor outcomes often obtained, meant that depression became an early focus for the development of evidence-based approaches to treatment. This can be seen in the fact that in the field of mental health most of the guidelines developed to date have been focused either on depression or schizophrenia (Parry *et al.*, 2003). As will be seen in Chapter 2, a central driver in the development of collaborative care services for the treatment of depression (Simon, 2006) has been the limited success of early attempts to improve the uptake of evidence-based care, principally clinical guidelines (for example, Katon *et al.*, 1995). The evidence to date for the effectiveness of collaborative care will

be considered in detail in Chapter 2; the remainder of this chapter will consider some of the key elements of evidenced based medicine as they apply to the evaluation and synthesis of complex healthcare interventions such as collaborative care.

The past 20 years have seen a major expansion of evidence-based medicine and it now assumes an increasingly important role in the work of healthcare professionals. Evidence-based medicine has been defined as "integrating individual clinical expertise with the best available external clinical evidence from systematic research" (Sackett *et al.*, 1996). In arguing for its development, Sackett and colleagues point to the substantial variation in clinical practice that exists in all healthcare systems and the considerable difficulties clinicians face in attempting to keep up with the relevant research from scientific and medical journals. For example, consultant physicians might be expected to read approximately 19 articles per day, 365 days per year to keep pace with relevant primary research in their field. This contrasts with the 1 hour per week that most consultants spend on reading primary research (Davidoff *et al.*, 1995). The challenge in properly reviewing, synthesising and evaluating relevant evidence was one of the reasons behind the establishment in 1999 of the National Institute for Health and Clinical Excellence (NICE 2005a) by the Department of Health in England. The establishment of similar organisations has now become common in most of the developed healthcare systems in the world (Parry *et al.*, 2003).

Evidence-based medicine increasingly draws on a global database, reflecting the international nature of much of the large-scale evaluation of healthcare interventions, which remain predominantly focused on pharmacological interventions. In parallel, journals have evolved that are specifically devoted to evidence-based medicine, for example, *Evidence-Based Medicine* and *Evidence-Based Mental Health*. This international evidence base has significant strengths, including making possible large-scale trials with adequate power so that moderate but important differences between treatments can be identified; it also supports the generalisability of the results (Peto *et al.*, 1995). The advantages of this approach are perhaps easiest to demonstrate for relatively simple interventions such as the use of aspirin following a myocardial infarction or of tamoxifen in the treatment of breast cancer (Peto *et al.*, 1995). However, for more complex healthcare interventions, such as a cardiac rehabilitation programme

(Jolly *et al.*, 2006) or a complex mental health intervention such as assertive community treatment (Killaspy *et al.*, 2006), an understanding of the healthcare system and specific service characteristics that might impact on the outcomes of a trial are vital to a proper interpretation and application of the evidence from the trial. The challenges this presents to the evaluation and understanding of complex interventions such as collaborative care and how they might be addressed are a central concern of this thesis. Before addressing this issue directly, the most prominent of the approaches used by national and international organisations to review, synthesise, evaluate and disseminate evidence will be reviewed below.

### 1.3 Clinical guidelines

In most healthcare systems the best-developed manifestations of evidence-based medicine are clinical guidelines, which are defined as 'systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances' (Field & Lohr, 1990). The purposes of clinical guidelines have been set out by NICE (2007). They are based on the best available evidence and are expected to promote both clinically efficacious and cost-effective care. They seek to directly improve the delivery and outcomes of healthcare by providing recommendations for treatment and care, thereby setting standards for treatment to guide healthcare professionals' behaviour. Indirectly, guidelines may also contribute to the education and training of healthcare professionals. They can be adapted (and often are) to help patients make informed decisions about their own care as well as improving communication between patients and professionals (NICE, 2007). They may also be used by healthcare commissioners and managers to guide the purchasing of services, develop the service structures by which to deliver effective healthcare and develop systems for the monitoring and evaluation of services. However, they have their weaknesses, often stemming from the limitations of the evidence base from which they are drawn and therefore can not be a substitute for the knowledge, skills and judgments of professionals (Sackett *et al.*, 1996).

Initially, clinical guidelines were mostly developed by specialist uni-professional groups, for example by groups of specialist physicians such as cardiologists or neurologists. Grilli and colleagues (2000) in a systematic review of "specialty

guidelines" (that is, those developed by uni-professional groups) focused on three areas of guideline development: professional and stakeholder involvement; identification of primary evidence; and appropriate grading of recommendations. They highlighted some of the potential problems with this specialist uni-professional approach. For example, of the 431 speciality guidelines they reviewed, only 5% were rated as adequate in terms of the search strategies used, the structure of the guideline development groups and the grading of recommendations. Grilli and colleagues argued that this demonstrated the need for a multi-disciplinary approach with explicit and transparent methods based on international standards of good practice. Recent trends in guideline development have supported this view and the recent significant international expansion of evidence-based medicine has often been based in multi-professional guideline development programmes such as the National Institute for Health and Clinical Excellence (NICE) in England and Wales, the Scottish Intercollegiate Guidelines Network (SIGN) in Scotland and the Agency for Healthcare Research and Quality (AHRQ) in the US (Parry *et al.*, 2003).

In their development, clinical guidelines rely heavily on two main methods for the identification and aggregation of data from primary research, namely the systematic review and meta-analysis, both of which are briefly described below.

*Systematic reviews*

The major method by which evidence for clinical guidelines is identified and evaluated is the systematic review. Systematic reviews usually summarise large bodies of evidence, which they achieve by synthesising the results of multiple primary investigations by using strategies designed to reduce bias and random error (Egger *et al.*, 2001). In well-conducted systematic reviews these methods are pre-defined and presented in a reliable, transparent, and reproducible manner (Egger *et al.*, 2001). They clearly specify the means by which studies will be identified, selected for inclusion, appraised and their results aggregated, and include steps to minimise bias at each of these stages. In most systematic reviews of the efficacy of a clinical intervention, the randomised controlled trial (RCT) (regardless of the results) is the preferred building block (Starr & Chalmers, 2003). A systematic review usually, but not always, contains a quantitative synthesis of the results. In some cases such a synthesis of the data might not

be possible. For example, this can occur where the designs of the included studies are too different for an average of their results to be appropriate (such as may occur when combining data from individual or cluster randomised trials without data available to allow for adjustments to take into account the effects of clustering); if the outcomes are not adequately reported; or where the difference in the nature of the outcome measures is too great to allow for a direct comparison. The quantitative analysis arising from a systematic review is usually referred to as a meta-analysis, although a meta-analysis can also be performed without a systematic review, simply by combining the results from more than one study.

The major difficulties that arise in the interpretation and use of systematic reviews in supporting clinical decision making derive from the difficulties in the methods used to identify, select and critically appraise the relevant studies. For most well-conducted systematic reviews, a well-designed electronically-based search strategy is required, which includes clearly specified search terms relevant to the subject under review and which searches relevant databases such as MEDLINE, EMBASE and PsycINFO. The development of these strategies is well described in a number of publications (for example, Egger *et al.*, 2001) and any well-conducted review should report on the number of relevant studies identified at each stage of the search and appraisal process (Moher *et al.*, 1999). However, even the best-designed search strategies have their limitations. When searching for efficacy studies these include the inability of the search strategies to fully compensate for the consequences of bias in publication (for example, the presence or absence in the review of unpublished studies or the selective reporting of outcomes), limitations of the MeSH (Medical Subject Headings) terms used in the descriptions of some studies and the delay in entering recently published studies onto relevant databases. Solutions to the latter two problems can be addressed to an extent by hand searching of the references of identified studies and the regular updating of the searches during the course of a review, but the problem of publication bias presents a much greater challenge.

The extent of the problems presented by unpublished studies can be seen in the systematic review by Whittington and colleagues (2004) that compared the clinical recommendations to be made about the use of selective serotonin reuptake inhibitors

(SSRIs) for children and adolescents with depression, based on both published and unpublished clinical trials of these drugs. Whittington and colleagues (2004) clearly demonstrated that if published studies alone had been used, a systematic review would have supported a widespread use of these drugs with few concerns being raised about the potential increased incidence of suicidal ideation in this very vulnerable group. The use of unpublished studies (which were obtained by Whittington and colleagues [2004] from the UK medicines regulator, the Medicines and Healthcare products Regulatory Agency [MHRA]) led to a very different outcome, with all but one of the SSRIs (fluoxetine) being identified as having an unacceptable harm/benefit ratio. This problem of selective reporting of trial outcomes has been confirmed in a number of studies, which have demonstrated that the inclusion of previously unpublished data may significantly alter the outcomes of a systematic review. For example, Melander and colleagues (2003), in a review of trials of SSRIs submitted to the Swedish medicines regulatory authority, demonstrated that studies with significant results were more likely to be published than those with non-significant results.

Another source of bias may arise from investigator allegiance. This can be seen in a number of studies of pharmaceutical industry sponsorship, including studies by Lexchin and colleagues (2003) and Perlis and colleagues (2005). Perlis and colleagues reported that company-sponsored trials were 4.9 times more likely to report a positive outcome for a particular drug than non-industry-sponsored studies. Much of the focus of this work has been on the bias introduced into clinical research by the commercial interests of the pharmaceutical industry. But it would be incorrect to assume that non-industry-sponsored trials (including trials of psychological or service interventions) are free from publication bias. Jacobson and Hollon (1996) in a discussion of the Elkin and colleagues (1989) trial of pharmacological and psychological treatment for depression also raised the possibility of investigator allegiance as a factor that may have influenced the outcome of the trial. In a well-conducted review Chan and colleagues (2004) demonstrated how the outcomes in final trial reports often differed from those set out in the original protocols (including many non-pharmacological trials) and resulted in a bias towards the publication of significant results. They suggested that this problem could be addressed by the registration of trial protocols when the trial is established and that subsequent publication of the trial outcomes be assessed against the original protocol. A

more immediate solution to the problem of publication bias that is commonly used in systematic reviews where quantitative synthesis of data is undertaken is to use a funnel plot (Egger *et al.*, 1997a), which is a statistical technique that can be used to identify potential bias by estimating the expected distribution of published and unpublished studies from an analysis of the published data.

*Meta-analysis*

The term meta-analysis was first defined by Smith and Glass (1977) to mean the statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings. Although the origins of meta-analysis were in the field of education and psychotherapy research, the approach was rapidly taken up in other areas. Meta-analysis is a statistical technique for the aggregation of the results obtained from a series of individual studies usually by identifying a common metric, an effect size often in the form of a standardised or weighted mean difference. In this review, meta-analysis is taken to have this "narrower" statistical definition, although in some cases meta-analyses are also understood to involve a systematic review. In evidence-based medicine the general aims of meta-analysis have included: providing more precise estimates of overall treatment effects; evaluating the impact of particular interventions on specific, often pre-selected, subgroups of patients; overcoming the difficulties of limited statistical power as a result of small individual trials; assessing safety or rare adverse events; providing improved estimates of the dose-response relationship; and appraising the impact of apparently conflicting study results (Egger *et al.*, 2001). Well-conducted meta-analyses allow for a more objective appraisal of the evidence, thereby reducing uncertainty and disagreement. Although meta-analysis brings greater precision than the analysis of any one of the component trials, it is still subject to any biases that arise from the study selection process (as discussed above) and inappropriate combining of results such as the use of different outcomes measures, trial populations or follow-up periods. All could lead to a precise, but clinically misleading, result.

Concern has also been expressed that the meta-analytic approach to evidence produces advice relevant to the care of a "mythical" average patient and thereby ignores important clinical and scientific evidence of relevance to the care of an individual

(Djulbegovic *et al.*, 2000; Kravitz *et al.*, 2004), and also ignores potentially important heterogeneity in the outcomes of clinical trials. Djulbegovic and colleagues (2000) are also concerned that the systems for grading or ranking evidence (with the meta-analysis of RCTs at the top of the hierarchy) can also lead to inappropriate treatment strategies. Sackett (1995) provides a thoughtful response to these points in a paper entitled "Applying Overviews and Meta-analyses at the Bedside", in which he skillfully describes how clinical judgement, and knowledge from meta-analyses and clinical practice, can be combined for the benefit of patients.

In recent years there has been a significant growth in the number of published meta-analyses. Delgado-Rodriguez (2006) reports that the number of references identified using the key word 'meta-analysis' has increased steadily from 329 in 1990, to 1649 in 2000 and to 2545 in 2004. There have been considerable criticisms of meta-analysis (for example, Oakes, 1986), and not least from Glass himself (Glass, 2000) who argued that the meta-analysis of individual studies should essentially be seen as an interim technological solution to the problem of the analysis of large data sets, which will eventually be improved on by the analysis of individual subject data sets. Others have drawn attention to the poor quality of many meta-analyses (for example, Delaney *et al.*, 2005) and this has led to attempts to improve the way systematic reviews and meta-analyses are conducted. The publication of the Quality of Reporting of Meta-analyses (QUOROM) statement (Moher *et al.*, 1999) was a response to these types of criticism and it set out a rigorous methodology to be followed in any meta-analysis, covering the preferred ways to present the abstract, introduction, methods, results, and discussion sections. It also sets out standards for searches, selection of papers, validity assessment, data abstraction, description of study characteristics, and quantitative data synthesis.

### 1.4 Challenges in the dissemination of evidence based medicine

The rapid development in methods for synthesising data from clinical trials presents a challenge for the dissemination of the evidence and recommendations generated. The Cochrane Collaboration (www.cochrane.org) was launched in 1993 and is the leading centre for the systematic aggregated evaluation of healthcare interventions. It has an international presence (there are 13 Cochrane centres based in countries including South Africa, the US, Brazil, Italy, Canada, the United Kingdom, Holland, Denmark and

France) and an explicit aim of disseminating results globally. On a quarterly basis its library publishes the results of all Cochrane reviews developed in over 50 diagnostic or topic-based editorial groups across the world. The benefits of such an approach are clear: it meets the requirements to consider the broadest range of interventions possible and by drawing on an international evidence base it promotes ownership across a range of healthcare systems. For many interventions, such an approach may present no difficulties. For example, in certain medical conditions such as ovarian cancer or chronic obstructive pulmonary disease, both of which can be treated by clearly defined surgical and/or pharmacological interventions, it is unlikely that the specific technical or pharmacological aspects of the intervention and their immediate outcomes will be significantly influenced by the country in which they are delivered (although the availability of resources may well limit access). But in other cases the use of drugs or surgical interventions may vary according to the population treated, for example, the different body fat distributions between women from Western Europe and North America and women from Southeast Asia have important implications when evaluating the efficacy of long-acting reversible contraception (NICE, 2005b).

### 1.5 Problems with the evaluation and dissemination of complex interventions

While problems in the dissemination and adoption of evidence-based medicine with many drug treatments may be limited, more significant problems arise when considering the international applicability or generalisability of healthcare interventions such as complex psychosocial interventions (for example, the collaborative care model for the treatment of depression [Simon, 2006], which is the central focus of this thesis) or team-based interventions (for example, specialist teams for the treatment of first-episode psychosis [Craig *et al.*, 2004]). Complex interventions have been defined by the Medical Research Council (2000) as interventions that are composed of a number of components that may act both independently and interdependently.

Understanding and interpreting evidence about complex interventions across healthcare systems not only requires an understanding of the different healthcare systems but also of the limitations of current research methods for evaluating these interventions. The limitations of the RCT, particularly as they apply to complex interventions, are discussed below. Problems encountered when evaluating findings from different

healthcare systems are also discussed, with the focus on complex interventions in mental health services research, because the problems of integration of data from international studies in this area are considerable. An understanding of these issues will help to clarify the evaluation of existing international research in collaborative care for depression and the design of further research into collaborative care in different healthcare systems from those in which it was originally developed.

*The randomised controlled trial and complex interventions*

The RCT is the accepted "gold standard" for the evaluation of therapeutic efficacy (Moher *et al.*, 1995), and although there are circumstances where its use may not be appropriate (for example, where the important outcome is a very low frequency event, where the disorder has a very low prevalence and recruitment may be problematic, or where obtaining informed consent is not possible), few would dispute its primacy in the evaluation of most healthcare interventions. Nevertheless, some challenges remain with the use of RCTs in the evaluation of complex healthcare interventions. This has been the subject of considerable controversy in the field of mental health, particularly in the area of psychological interventions (for example, Seligman [1995], Persons & Silberschatz [1998] and Wilson [1998]).

The challenges presented by the use of RCTs in the evaluation of psychological therapies include: problems of the populations involved in trials (including the absence of the multiple comorbidities seen in routine practice), the focus on narrow definitions of outcomes (for example, symptoms rather than quality of life), and the lack of external or ecological validity (Persons & Silberschatz, 1998). In addition, RCTs also have limitations in determining how and why treatments are effective (for example, Kazdin, 2007). Many of these problems are similar to the problems encountered in the development of clinical practice guidelines and have been summarised by Pilling and Price (2006); they include:

*The nature of patient populations* – RCTs, by their nature, require high internal validity and therefore often include precisely specified populations (for example, "pure" diagnostic groups). This may lead to trial populations that are unlike those encountered in routine clinical practice. It is well established in the field of mental health that the

comorbidity of disorders is often the norm. For example, over 50% of people with a depressive disorder also have significant comorbid anxiety (Goldberg *et al.*, 2005) and 40% of people with post-traumatic stress disorder may also be suffering from a depressive disorder (Ehlers *et al.*, 2005). This apparent lack of comparability of trial and routine care populations is often cited as a reason by clinicians for the lack of uptake of evidence-based medicine (Sackett *et al.*, 1996). However, it should be remembered that comparisons are relative (both experimental and comparator groups are from the same select population). In addition, there is an emerging evidence base in the field of mental health that comorbidities do not necessarily prevent patients benefiting from particular interventions. Recent research suggests that individuals with significant comorbidities, such as personality disorder, can benefit from structured psychological treatments for disorders such as anxiety and depression (Arntz, 1999). Arntz (1999) also acknowledges that such treatments may not directly affect the problems associated with personality disorder and some extension of the normal duration of treatment may be required (for example, Ehlers *et al.*, 2005). Mulder (2002), in a review of the effects of personality factors on outcomes in major depression, also concluded that the presence of personality problems should not be seen as an inevitable impediment to the effective treatment of depression. Further data, which casts some doubts on the magnitude of the problem that this presents in the interpretation of RCTs, comes from studies such as that by Franklin and colleagues (2000) who, in a treatment study of individuals with obsessive-compulsive disorder (OCD), demonstrated that those who had previously been excluded from clinical trials of OCD because of comorbidities and other related problems benefited as much, if not more, than those in the original trials.

Wilson (1998) summarised a similar evidence base for patients suffering from a range of anxiety disorders where the outcomes were again comparable for non-selected clinic patients to those obtained in clinical trials. In another approach to looking at problems encountered in routine practice, Gray and colleagues (2007) compared the outcomes for panic disorder obtained in routine practice by counsellors working in primary care before and after limited additional training. They showed that with the provision of treatment and supervision in line with standard trial protocols (for the delivery of cognitive behavioural therapy [CBT] for panic disorder) and supported by good

supervision, counsellors were able to significantly improve outcomes and bring them in line with those obtained in clinical trials.

*The outcomes used and the duration of follow-up* - the current use and reporting of outcomes in RCTs presents several problems for psychological treatment trials and health service research. A major criticism is the reliance on symptomatic measures as primary outcome measures, for example, scores on depression or anxiety rating scales, which are effectively proxy measures of the disorder and which may lend themselves more easily to the demonstration of efficacy than some categorical measures such as the presence or absence of the disorder (Kirsch & Moncrieff, 2007). Given the chronic nature of many mental disorders and the reports from patients of the burden of illness, there is a strong argument that measures of interpersonal, social and occupational functioning should be given much more prominence as primary outcomes, but unfortunately this is not often the case (Pilling & Price, 2006). The use of measures of social and personal functioning would also facilitate more reliable assessments of the cost effectiveness of interventions, an element often missing from many RCTs.

RCTs of psychological and other complex interventions are costly to deliver and there are inherent difficulties with maintaining blindness and integrity of the interventions. One consequence is that the duration of follow-up after the completion of the interventions is often short (for example, less than 6 months), which presents a particular problem with chronic disorders such as depression or schizophrenia that often have a relapsing and remitting course. Most noticeably the absence of long-term follow-up can lead to an over-estimation of treatment effects. This is evident in the meta-analysis conducted by Westen and Morrison (2001), which focused on short-term and long-term outcomes of psychological treatments for panic disorder, generalised anxiety disorder and depression. They showed that while good results were obtained in both the short term and long term for panic disorder, this was not the case for either depression or generalised anxiety disorder. Lack of long-term follow-up studies may also limit the information that is reported on the potential harms associated with an intervention. This can be seen, for example, in the evidence that has emerged in recent years on the association of weight gain with the use of atypical antipsychotics for the treatment of

schizophrenia. It was initially expected that the atypicals would significantly reduce side effects (predominantly extrapyrimidal side effects) while delivering at least the same clinical benefits (Geddes *et al.*, 2000a). While the reduction of extrapyrimidal side effects has been confirmed, it has become apparent that atypical antipsychotics are often associated with significant weight gain and possibly also diabetes (Jin *et al.*, 2004; Nasrallah *et al.*, 2006). Inevitably, if an associated harm is prominent and easily observed an intervention will not proceed to the level of an RCT for evaluation but significant harms may be low-frequency events and require longer-term follow-up or meta-analysis to identify them. (Indeed it could be argued that for some harm data, cohort studies and post-implementation surveillance are more appropriate methods than an RCT.)

*The comparators used in trials* - understanding the efficacy of an intervention crucially depends on an understanding of its comparator. In some cases this can be a relatively straightforward matter where the comparator is an alternative drug. However, many complex interventions and their comparators are often inadequately described. Terms such as "treatment as usual" or "usual care" for comparators are often assumed for the purposes of meta-analysis to be equivalent, but such an assumption may mean that considerable differences are ignored with a consequent misinterpretation of the results. For example, a Dutch study of collaborative care for depression (Smit *et al.*, 2006) had a control group receiving "care as usual" in primary care, which comprised a wide range of interventions from practice-based staff including antidepressant treatment and long-term psychological interventions. In addition, participants in the "care as usual" arm were also free to use other primary or secondary care mental health services outside the practice and did so in significant numbers. This is considerably different from what typically constitutes usual care for depression in the UK (Goldberg *et al.*, 2004). Perhaps not surprisingly, the usual care group in Smit and colleagues (2006) had a high level of compliance with antidepressants and no significant difference in the use of primary mental health services, but a significantly higher use of other specialist mental health services. In a similar vein, an examination of the influential RCT by Elkin and colleagues (1989) of psychological and pharmacological interventions in the treatment of depression reveals that the antidepressant arm of the trial consisted not simply of the prescription of antidepressant medication but also the provision of "clinical

management". Clinical management consisted of weekly sessions with a psychiatrist lasting 20 minutes and the availability of 7-day a week, 24-hour a day crisis interventions. Such an intervention is very different from what is routinely provided in outpatient depression care in either the US or the UK (Goldberg *et al.*, 2004) and suggests that to describe the trial simply as a comparison of antidepressants and psychological therapies is misleading. Albon and Jones (2002) in a comparative content analysis of the components of the two psychological interventions (CBT and interpersonal therapy) used in the trial by Elkin and colleagues (1989) argue that the difference is essentially one in name only and that both treatments provided what might be more appropriately defined and understood as CBT (Beck *et al.*, 1979). While Albon and Jones' conclusions may be disputed, their paper serves to illustrate an important point: careful reporting and monitoring of all the intervention arms of a trial is important if the results of the trial are to be properly understood. Other commentators on the work of Elkin and colleagues (1989) have raised concerns about the quality of the treatments delivered, citing potential differences in the competence of the therapists delivering CBT as being a possible factor in accounting for its lack of effect with more severely depressed patients in the trial (for example, Jacobson & Hollon, 1996).

*The moderators and mediators of treatment effects* – despite the limitations set out above RCTs have been successful in establishing the efficacy of psychological interventions (Roth & Fonagy, 2005). However they have been far less successful in establishing the mechanisms by which the changes brought about in treatment are achieved (Kraemer *et al,* 2002; Kazdin, 2007). Kazdin (2007) in a helpful discussion of the limitations of current research methods draws a distinction between mediators (an intervening variable which may account for the relationship between independent and dependent variables), mechanisms (the basis of any effect, that is the means by which change is brought about) and moderators (a characteristics that may influence the direction or magnitude of the relationship between independent and dependent variables). Kazdin argues that understanding these mechanism of change, as defined above, is important because it may bring several advantages which include a reduction in the complexity of interventions; clarification of the key outcomes; novel methods to support generalisation to routine clinical practice; identification of potential moderators

of treatment effects and support for the development of better theoretical models of treatment and /or the disorders they are designed to treat (Kazdin, 2008).

Kazdin also sets out a number of refinements to RCT method which are needed to support the identification of the mechanism of change in RCTs. These include increased use of theory to generate hypotheses about the mechanisms of change; specific measures of potential mediators in treatment trials; the establishment of a 'timeline' (that is a process for assessment of both mediator and outcomes which support analysis of the potential causal relationships between them) and the use of routine session by measurement of both outcomes and mediators. He also argues for the use of a broad range of methods, in addition or in combination with RCTs, including laboratory studies, underlying biological mechanisms and detailed observational studies all of which can converge to help clarify the mechanism of change. Such an approach will require significant refinement not only of trial design (Kraemer *et al,* 2002; Kazdin, 2007) but also in methods of analysing trail data (Laurenceau *et al*, 2007).

*Comparisons across healthcare systems*

The problems described so far have concentrated on the limitations of RCTs, particularly in their construction and interpretation. Even if comparisons are limited to the developed world, for example the socialised medical system of the NHS in the UK or the largely privatised system for the delivery of healthcare in the US, differences can be considerable particularly when characterising "treatment as usual" or "usual care". Importantly from the perspective of this thesis, differences in healthcare settings, particularly in relation to complex interventions, can have a significant impact on the interpretation of results from clinical trials. This problem can be compounded when the majority of trials of a particular intervention are conducted in one type of healthcare system but the results are then extrapolated to another.

Over the past 10 years the English NHS has seen the development of mental health policy driven by the "functional team" model (Department of Health, 1999), which specifies that certain functions, for example, the management of patients in crisis, should be provided by specialist or functional teams. The National Service Framework (Department of Health, 1999), which sets out this functional system, drew explicitly on an international evidence base to support the policy development. The potential

problems with this approach are illustrated below with a discussion of the evidence base underpinning two key components of the functional approach to the provision of community mental health services: crisis intervention and home treatment teams, and assertive community treatment. Both crisis intervention and assertive community treatment have been central to mental health policy and are now in some form or another part of most community mental health services in England (Appleby, 2004).

In the case of crisis intervention and home treatment teams, the evidence base on which the policy was developed is summarised by Joy and colleagues (1998).They describe five studies, which included 724 patients, but which all varied significantly in the way in which the crisis intervention and home treatment teams were constructed and in the comparators used. Only one UK-based trial was included, with one from Australia and three from North America. Joy and colleagues were unable to identify any consistent evidence supporting the efficacy of crisis intervention and home treatment teams and concluded their review by stating:

> "Home care crisis treatment, coupled with an ongoing home care package, is a viable and acceptable way of treating people with serious mental illnesses. If this approach is to be widely implemented it would seem that more evaluative studies are needed."

It should be noted that the one UK study, Muijen and colleagues (1992), did not report a significant result on a key outcome (prevention of readmissions to hospital). Therefore a reading of the data would suggest that the adoption of crisis intervention and home treatment teams by the UK Department of Health was premature. (However, it should be noted that two more recent positive trials of UK-based crisis intervention and home treatment teams [Johnson et al., 2005a & b] suggest that despite the weak evidence base the Department of Health may have been correct and were perhaps fortunate in their recommendation.)

In contrast, the evidence base for assertive community treatment was apparently much stronger, with a series of positive findings summarised in Marshall and Lockwood's (2000) review of 22 trials. Given the evidence base, they concluded that assertive community treatment is:

> "....a clinically effective approach to managing the care of severely mentally ill people in the community. Assertive community treatment, if correctly targeted on high users of in-patient care, can substantially reduce the costs of hospital care whilst improving outcome and patient satisfaction. Policy makers, clinicians, and consumers should support the setting up of assertive community treatment teams."

However, it should be noted that the review drew on 22 clinical trials all bar two of which were from North America, the others being from the UK and Sweden. As with crisis intervention and home treatment teams, the sole UK study (Audini *et al.*, 1994) showed no difference on the key outcome measure (admission to hospital during the study), with both experimental and control groups having identical admission rates, and the other European study (Aberg-Wisedt *et al.*, 1995) reporting no data on this important outcome. In contrast to more recent findings on crisis intervention, a recent large-scale trial of assertive community treatment in the UK (Killaspy *et al.*, 2006) suggested that this time the Department of Health may not have been so fortunate; 18-month follow-up data demonstrated no difference in hospital bed use between assertive community treatment and care provided by standard community mental health teams.

What then can explain these differences between the UK and the US, particularly when investigators go to considerable efforts to ensure that the experimental intervention is provided in a consistent manner? For example, most recent assertive community treatment trials used a "fidelity measure" (Teague *et al.* 1998) to assess whether they were providing an intervention consistent with the proposed model. Its use, at least in assertive community treatment in the UK (Killaspy *et al.*, 2006), would suggest that this is the case (Wright *et al.*, 2003) and that the problem of different outcomes may lie not with the model of care provided in the experimental condition but in the control condition or comparator. A possible explanation can be found in the quality of comparator care provided; in the US, care for the severely mentally ill is generally accepted to be of poor quality and uncoordinated (Wang *et al.*, 2002), with limited provision of the type of standard multi-disciplinary care common in the UK (Department of Health, 1999).

### 1.6 Making use of evidence: guiding, affirming or challenging policy

The above discussion raises questions about the impact of evidence-based medicine on policy decisions and the provision of mental health services. The studies by Johnson and colleagues (2005a & b) suggest that the approach taken by the Department of Health in the UK may have been correct in the case of crisis intervention and home treatment teams but possibly mistaken in the case of assertive community treatment (Killaspy *et al.*, 2006). Such decisions have considerable implications for both the financial and clinical integrity of NHS mental health services.

However, Department of Health policy does not stand still and a further area of mental health policy is currently enjoying considerable support. This is the provision of collaborative care (or enhanced care) for depression (Von Korff & Goldberg, 2001; Simon *et al.*, 2000), a complex health service intervention that was first developed in the US. It emerged from the development of chronic disease management systems in physical disease (Von Korff *et al.*, 1997) and there is a substantial evidence base in the US to support its efficacy (Gilbody *et al.*, 2006a). As yet there have been no UK-based formal evaluations of collaborative care of depression that have reproduced the results obtained in the US. However, this has not prevented Simon (2006) advocating, in a recent *British Medical Journal* editorial, that the collaborative care model for the treatment and management of depression should be widely adopted throughout the UK healthcare system since the evidence of its efficacy has been convincingly demonstrated. The validity of Simon's assertion is a central concern of this thesis because it raises a direct question about the transferability of a complex intervention between different healthcare systems. Consequently, the evidence for collaborative care will be reviewed along with a consideration of the efficacy of its component parts, in order to support the development and evaluation of a feasibility trial of collaborative care in the context of primary care mental health services in the UK National Health Service.

# 2. Collaborative Care for Depression

## 2.1 Introduction

This chapter reviews the development of collaborative care for depression. It begins with a consideration of the origins of the model in the chronic care of physical illness and reviews the evidence for this approach. Other relevant literature from the area of guideline implementation and organisational change is reviewed before considering the implications of the multi-factorial aetiology of depression and the evidence for the effectiveness of collaborative care for depression. This chapter concludes with a discussion of the limitations of the current evidence base for collaborative care and its application to the development of collaborative care for depression in the NHS.

The origins of collaborative care for depression developed in significant part from the failure to bring about improvements in line with the standards set out in clinical practice guidelines for depression (for example, Katon *et al.*, 1992). This failure was part of a more general pattern of poor outcomes for people with depression and other common mental disorders (Donoghue and Tylee, 1996; Young *et al.*, 2001). These led investigators to consider what lessons might be learnt from other areas of medicine, in particular chronic diseases such as diabetes (Von Korff *et al.*, 1997). This approach is often referred to as the chronic care model and its development is described below.

## 2.2 The development of the collaborative care model

Before describing the development of the collaborative care approach to depression, the conceptual and theoretical underpinnings of the model as developed for the care and treatment of chronic physical illness will be described below. This is followed by a consideration of other relevant literature on organisation change and development and the multi-factorial nature of depression.

### The chronic care model

The chronic care model is one of a number of similar terms including "disease management programme" and the "chronic disease model" that describe an approach to the management of chronic disease that has developed in the last 15 years (Von Korff *et al.*, 1997). The model emerged as a response to a general dissatisfaction with healthcare

outcomes for people with chronic health problems, particularly in the US (see, for example, the influential Institute of Medicine report "Crossing the Quality Chasm" [Institute of Medicine, 2001]).

The chronic care model focuses on the treatment and management of chronic conditions, which are defined as illnesses that last longer than 3 months and are not self-limiting (Von Korff *et al.*, 1997). Although developed originally for diseases such as diabetes, coronary artery disease, hypertension, and chronic obstructive pulmonary disease (Renders *et al.*, 2001; Bodenheimer *et al.*, 2002), the model has now been applied to a wider range of disorders such as multiple sclerosis, depression, and osteoporosis (Wagner & Groves, 2002; Tsai *et al.*, 2005). Given the chronic nature of much depression (perhaps 50% of cases recur and many people become chronically depressed or experience only partial remission and, as result, suffer from continuing impairment of function [Goldberg *et al.*, 2004]), it is possible to see why the chronic care model could apply to depression. Chronic diseases have been estimated to affect almost half of the US population (Von Korff *et al.* 1997) and account for approximately three quarters of healthcare costs in the country (Hoffman *et al.*, 1996).

In addition to the financial burden presented to the wider society by chronic illness there is also a recognition that the responsibility for everyday care rests mostly with patients and their families. It therefore follows that for many patients effective collaborative relationships with healthcare providers can help them and their families better cope with many of the challenges to everyday living presented by their illness (Von Korff *et al.*, 1997). The model of care that follows from this is one that focuses on enhancing self-care in chronic illness, while at the same time ensuring that effective medical care is provided. Von Korff and colleagues (1997) set out what they see as the four essential elements of collaborative care:

1. The collaborative definition of problems, in which patient-defined problems are identified alongside medical problems diagnosed by healthcare professionals.
2. The focus on specific problems where targets, goals and plans are jointly developed between patients and professionals to achieve a set of realistic objectives in the context of patient preferences and readiness.

3. The creation of a range of self-management training and support services, in which patients have access to services that teach the necessary skills needed to carry out treatment plans, guide behaviour change, and provide emotional support.
4. The provision of active and sustained follow-up, in which patients are contacted at specified intervals to monitor health status, identify potential complications, and check and reinforce progress in implementing the care plan.

Von Korff and colleagues (1997) argue that these four elements, which focus very much on the individual level of care, make up a common core of services for potentially all individuals with chronic illness and do not need be reinvented for each disease or disorder.

This emphasis on the development of programmes to support individual patients in self-management of their chronic illness has been matched by an increasing concern to improve the organisational structures in which care is delivered. The literature, which is heavily influenced by the Seattle group (including Edward Wagner and Michael Von Korff), sets out what organisational structures should be in place to support the effective implementation and maintenance of the chronic care model. This approach has a number of key elements, summarised by Kilbourne and colleagues (2004), and include:

1. Leadership – that is the provision by an individual (or in order to support sustainability, more than one leader) of the vision, resources and accountability to maintain the effort required to deliver the requisite change. Key tasks of the leaders include: continued educational input to the setting, engagement with and addressing the concerns of stakeholders, monitoring key process and outcome indicators, providing feedback and ensuring effective communication.
2. Decision support – this is concerned with providing clinicians with the necessary advice and information to deliver optimal care. Often this is in the form of evidence-based clinical guidelines or protocols for the delivery of an intervention. (In depression-focused chronic care, the stress is not only on the protocols to deliver effective care but also the tools that might be used in case identification, given the large number of people with depression who go

untreated [for example, Miranda *et al.*, 2003]). Typically protocols should be locally tailored to provide information on appropriate treatment, referral pathways for complex cases and mechanisms to track patients' progress. These protocols should be supported by access to regular training, routine reviews of barriers to implementation, review of staff structures and systems for routine staff–patient communication.

3. Delivery system design – here there are two main elements, the first of these being care management, which is the development of a specified non-medical role in the organisation that takes direct responsibility for the coordinating and, in significant measure, the provision of care. This would include developing a therapeutic relationship, providing psychosocial treatment, follow-up, developing a personal action plan, and monitoring treatment response and adherence. In a number of chronic disease areas this has led to the creation of specialist posts such as diabetes nurses (Piatt *et al.*, 2006) or depression care managers (Simon *et al.*, 2004). Secondly, Kilbourne and colleagues (2004) stress the importance of taking into account what they refer to as "behavioural health linkages", which essentially refers to the comorbidity that both characterises and complicates the care of many chronic physical disorders, for example depression and cardiovascular disease (Williams *et al.*, 2004).
4. Clinical information systems – in the chronic care model particular emphasis is placed on the use of disease registers (Wagner *et al.*, 2001). Kilbourne and colleagues describe the key characteristics of such registers, including ease of use, compatibility with existing financial and service monitoring systems, linkage with other aspects of the personal healthcare record and the ability to generate patient-relevant and accessible outputs. The data generated by the system then supports the central care planning and monitoring function of all clinical staff involved in the provision of care.

*The effectiveness of the collaborative care model*

The provision of collaborative care has been evaluated in a number of RCTs of chronic physical disorders. The outcomes of these trials are briefly reviewed, drawing on existing systematic reviews and related commentaries. This review is not intended to be comprehensive but rather to represent the range of outcomes obtained and some of the

problems encountered so as to inform the evaluation and development of a collaborative care intervention for depression.

McAlister and colleagues (2001) reviewed multidisciplinary disease management programmes (essentially collaborative care programmes) aimed at improving secondary prevention in patients with existing heart disease. They identified a total of 12 trials including almost 10,000 patients and concluded that disease management programmes improved the delivery of care, reduced hospital admissions and enhanced quality of life or functional status. However, the impact of the approach on mortality and further infarctions, cost effectiveness and the optimal composition of the interventions remained uncertain. Weingarten and colleagues (2002) in a systematic review of 118 disease management studies attempted to address one of the key questions raised by McAlister and colleagues (2001), that is what constitutes the effective components of such programmes. They identified a number of strategies used in the studies, of which the most common was patient education (92/118), followed by professional education (47/118) and feedback (32/118). However, most of the programmes (70/118) used more than one intervention. Education, feedback, and reminders were all associated with significant improvements in adherence to the relevant protocols, with effect sizes ranging between 0.44 (95% CI 0.19 to 0.68) and 0.61 (95% CI 0.28 to 0.93), and in patient-based outcomes, with effect sizes ranging between 0.17 (95% CI 0.10 to 0.25) and 0.35 (95% CI 0.19 to 0.51). However, the type and number of interventions varied greatly, and it remained unclear in the review which interventions were most effective. This review also covered mental health interventions (specifically those for depression) and noted that these studies reported on average higher overall benefits for both staff- and patient-based outcomes than any other disease condition. Studies focused on diabetes suggest that a stress on self-management may be associated with better outcomes (Renders *et al.*, 2001; Bodenheimer *et al.*, 2002). A systematic review by Shojania and colleagues (2006) suggested that certain interventions including team changes, case management and patient reminders were on average associated with better outcomes than clinician reminders and continuous quality improvement.

The above reviews suggest that collaborative care that has an explicit patient focus (for example, patient education or self-management) can bring about positive changes in

service usage, with impact also on patient functioning and quality of life, although the cost effectiveness of such interventions and impact on longer-term health outcomes remains uncertain. However, despite this generally positive picture, considerable concerns remain about the uptake of chronic care or disease management programmes in routine care, even in the best resourced of services in the US (Rundall *et al.*, 2002). More recently, studies conducted in the UK have also begun to throw some doubt on the effectiveness of the chronic care model for chronic physical health problems. This can be seen, for example, in the trial by Eccles and colleagues (2002) of computerised disease management systems to support the effective care of asthma and angina, where no benefit of the system was identifiable. Eccles and colleagues (2002) account for this lack of effect in terms of clinician workload and the complex comorbidities with which many patients present. Gravelle and colleagues (2007) also report no benefit for frail elderly people following the implementation of the "Evercare" system of community matron-based integrated healthcare, citing the lack of sufficient service redesign as the primary reason for its failure to bring about the benefits delivered by similar programmes in the US. The concerns raised by Rundall and colleagues (2002), Eccles and colleagues (2002) and Gravelle and colleagues (2007) echo those of Kilbourne and colleagues (2004), where service design or organisational failures were seen as a major reason why chronic care models for depression in routine practice were not delivering the outcomes reported in clinical trials. A number of commentators, for example Valdeck (2001), have supported this emphasis on service redesign, while others such as Coye (2001) and Bringewatt (2001), suggest that the major drive for change will come primarily from increasing cost pressures and consumer dissatisfaction. However, the failure to find a substantial benefit in the non-American studies (for example, Eccles *et al.*, 2002; Gravelle *et al.*, 2007) may reflect aspects of the healthcare system other than the lack of adequate service redesign, such as better provision of standard chronic care. Some support for this idea comes from the recent work by Michael Marmot and colleagues (Banks *et al.*, 2006) who reported that, despite significantly greater spending, outcomes for adults with chronic diseases in the US are on average worse than those in the UK.

## 2.3 The implementation of clinical guidance

The collaborative care model not only seeks to improve patient involvement in care but also to change professional behaviour and organisational culture. It follows therefore that a consideration of studies that have evaluated interventions in these areas may have implications for the evaluation and development of collaborative care interventions. One related area of importance is that of clinical guideline implementation, an area that has undergone considerable evaluation (Grol & Jones, 2000; Grimshaw *et al.*, 2004). Perhaps the most important message to emerge from the guideline implementation literature is that the majority of interventions to support implementation have only small to moderate effects. Grimshaw and colleagues (2004) in a large and comprehensive review of 235 guideline implementation studies were able to identify improvements in the desired direction in 86% of studies but the effects tended to be modest, falling broadly within the range of 6 to 14%, although a number of projects have reported higher rates of implementation, between 30 and 60% (Grol & Jones, 2000). Reminders to clinicians were consistently observed to be the most effective interventions with more limited effects reported for educational outreach, and variable but sometimes important effects for the dissemination of educational materials. Interestingly, the multifaceted approaches such as those often found in the chronic care model (Von Korff & Goldberg, 2001; Tsai *et al.*, 2005) were not necessarily more effective than single interventions. Audit and feedback and the use of opinion leaders were usually less successful in bringing about positive change – this is broadly in line with the chronic care model literature for physical health problems (Shojania *et al.*, 2006). One less encouraging aspect of implementation research on clinical guidelines is that the overall improvement is often much the same for poor performers as good performers, with the result that guideline implementation programmes may do little to reduce variation in practice, a finding common to the field of collaborative care (Rundall *et al.*, 2002).

The findings relating to guideline implementation are mirrored by those of a systematic review of organisational interventions to improve patient care by Wensing and colleagues (2006). Their review examined the impact of the following five organisational interventions:

1. Revision of professional roles; that is, change of tasks and responsibilities of health professionals, such as increased medical roles for nurses.
2. Increased use of multidisciplinary teams to improve professional performance and patient outcomes.
3. Integrated care services; that is, organised systems for the delivery of care (including disease management programmes but also integrated care pathways and case management) to patients with specific diseases.
4. Knowledge management; that is, the use of information and technology and communication systems to support patient care, such as computerised medical record keeping.
5. Quality management, which focuses on the patient as customer, with continuous efforts to improve, measure and analyse performance. Various approaches, such as total quality management, continuous quality improvement, and business redesign were included in this category.

Wensing and colleagues (2006) found that there was reasonable evidence to support improved professional performance when the focus of the interventions was on professional role revision or the use of computer systems both for reminding and decision support, particularly in preventive care. Interventions aimed at promoting multidisciplinary teamwork or the development of integrated care services also improved patient outcomes in chronic conditions and, in the case of integrated care, saved costs. Knowledge management also improved professional performance and patient outcomes across a range of conditions. Multiple interventions showed a range of positive effects, but the effects for quality management remained uncertain. Grol and Grimshaw (2003) reviewed a number of organisational interventions that were not covered by Wensing and colleagues (2006) including leadership, process redesign, organisational culture and organisational learning interventions. They concluded that there was no consistent evidence that supported the use of any one of the interventions over any other, but that all potentially could bring about positive benefits in patient care; however they raised questions about the sustainability of benefit if the interventions were not maintained.

As can be seen from the studies covered by Wensing and colleagues (2006) and Grol and Grimshaw (2003), there is some overlap with the type of interventions covered in the chronic care literature. When taken together with guideline implementation, there is a suggestion that organisational interventions such as clinician-specific reminders or educational interventions may be effective, as might the development of leadership programmes and new professional roles and multidisciplinary teams. However, uncertainty about the sustainability, long-term benefits and cost effectiveness of the interventions remain. Multifaceted approaches and the use of quality management programmes look less promising and this may arise from a lack of specificity or targeting of the change interventions in these programmes.

### 2.4 Developing a taxonomy to effect change

The relative lack of change associated with quality management programmes and multifaceted approaches, together with the absence of any clear hierarchy of effectiveness from single intervention studies, limits the conclusions that can be drawn about the effective components of chronic care interventions. A number of authors, including Wensing and colleagues (2006), have argued that the lack of an agreed taxonomy for organisational interventions presents significant problems in both developing and evaluating them. The development of such a taxonomy requires not only effective descriptions of the interventions but also ways of characterising the environment in which the interventions are set. The importance of this can be seen in a UK-based evaluation of the implementation of NICE clinical guidance (specifically the Technology Appraisal programme) by Sheldon and colleagues (2004). They reported variable uptake of a range of health technologies (primary pharmaceuticals and some surgical procedures), with the guidance more often being followed for pharmaceuticals (in particular, drugs for cancer and obesity) but with a lower uptake for a range of surgical procedures. Organisational factors associated with successful implementation included: strong professional support; effective professional management structures; and good financial and clinical monitoring systems.

The lack of a taxonomy for characterising change in organisational behaviour referred to by Wensing and colleagues (2006) is also mirrored in the lack of a taxonomy for changing health professionals' behaviour, despite the fact that many service improvement strategies focus on this area. Michie and colleagues (2005) argue that this

lack of a typology of health professionals' behaviour has significantly held back the development of effective strategies to support implementation. They have developed a typology of health behaviours, based on a systematic review of psychological theories of behaviour change, which they argue should form the basis of a typology of future studies to change behaviour[2]. This has been used in a number of pilot studies, including work on the style in which clinical guidelines are written (Michie & Johnston, 2004; Michie & Lester, 2005) and also on clinicians' attitudes and intentions regarding the implementation of specific guidance (Michie *et al.*, 2007). In their 2007 study, Michie and colleagues used the framework to examine the implementation of specific recommendations in the NICE schizophrenia guideline (Kendall *et al.*, 2002). The study demonstrated that the model can not only serve as a framework for developing an intervention but can also lead to a more precise directing of resources onto the skill or support needs identified by staff who are required to implement the intervention.

Understanding what constitute the effective elements of a complex organisational intervention is not only handicapped by the lack of appropriate typologies at the individual or organisational level but also by the absence of an overarching theoretical framework in which to integrate them. Ferlie and Shortell (2001), however, provide a multi-level framework in which it may be possible to begin to integrate the different levels of approach. They specify four levels: the individual health professional; the healthcare team; the organisation providing healthcare (such as an NHS trust); and the larger healthcare system (such as the NHS). They argue that change at any one level may require change at another level or, at a minimum, awareness of the change; therefore the adoption of the framework can guide the selection of the appropriate interventions at each level. For example, the framework might be applied to problems with the routine uptake of chronic care interventions reported by Rundall and colleagues (2002).

[2] These behaviours include: knowledge, skills, social/professional role and identity, beliefs about capabilities, beliefs about consequences, motivation and goals, memory, attention and decision processes, environmental context and resources, social influences, emotion regulation, behavioural regulation, and the nature of the behaviour.

## 2.5 The multifactorial aetiology of depression

Effective chronic care interventions tend to be focused on specific disorders such as diabetes, and the presence of complex comorbidities may impair their effectiveness (Eccles *et al.*, 2002). Depression is a broad and heterogeneous diagnostic grouping, central to which is depressed mood or loss of pleasure in most activities, based on the identification of a set of core symptoms and is often comorbid with other disorders such as anxiety (Goldberg *et al.*, 2004). In addition, there are significant limitations with the concept of depression itself, and a number of authorities concerned with the care and treatment of the condition (for example, NICE, 2004a; Parker, 2005) have questioned the validity of the concept, suggesting that it is too broad and heterogeneous and has only limited validity as a basis for developing effective treatment. A focus on symptoms alone is held not to be sufficient because of the range of biological, psychological and social factors that significantly impact on the aetiology and course of the disorder, and the response to treatment in depression. As these factors have an important bearing on the applicability of the chronic/collaborative care model to depression, they are briefly reviewed below.

The heterogeneity in the presentation, course and outcomes of depression is reflected in the range of theoretical explanations for its aetiology. While no single theory has been identified as accounting for the development of depression, it is broadly accepted that the disorder is multifactorial (Goldberg *et al.*, 2004), with genetic (Moffitt *et al.*, 2007), biochemical (Goodwin, 2000), psychological (Freud, 1917; Beck *et al.*, 1979), and social (Brown & Harris, 1978) factors all playing a part. How precisely these factors influence the course of the disorder in an individual is not well understood. Often the theories of the aetiology of depression have been driven by the response to treatment, for example, treatment with antidepressants and serotonergic theories of the causation of depression (for example, McAllister–Williams *et al.*, 1998).

The stress–vulnerability model of depression (Nuechterlein & Dawson, 1984) sets out a framework in which 'vulnerability factors' interact with current social circumstances, such as poverty or social adversity, and with stressful life events (including physical health problems) to trigger a depressive episode (Harris, 2000). A family history of depression is a significant predictor of vulnerability to the disorder (Kendler *et al.*,

2001), and a wide range of personal experiences such as a poor parenting (McLeod *et al.*, 2007), marital discord and divorce (Huurre *et al.*, 2006), and physical and sexual abuse (Gladstone *et al.*, 2004), may contribute to the development of depression. Epidemiological data (for example, Meltzer *et al.*, 1995a & b) also demonstrate the role of adverse social circumstances in increasing the risk of depression and also in maintaining a depressive episode (Brown & Harris, 1978). Although social factors may be powerful in triggering and maintaining depression, the disorder may occur in the absence of a stressful event; while factors such as having a supportive confiding relationship (Brown & Harris, 1978) can protect against depression following a stressful life event.

The multifactorial nature of depression would therefore suggest that effective interventions, including collaborative care, would have to consider the different aetiological and maintenance factors and further suggest that a broad range of pharmacological, psychological and social interventions may need to be available to treat the range of depressive disorders effectively. Put simply, programmes that focus only on one area of difficulty may have limited success.

### 2.6 Improving care for depression

The major focus of the attempts to improve care for people with depression in primary care has been through the provision of additional staff (Cape *et al.*, 2007). In the US the concentration has been on the development of the collaborative care model, but in the UK and elsewhere in Europe other models have been developed, notably the addition of mental health professionals to the primary care team (Bower & Sibbald, 2000). It should be noted that some of the early attempts to provide collaborative care in the US consisted of little more than a mental health professional attached to a primary care setting (for example, Kroenke *et al.*, 2000). However, there has been considerably more description and, importantly, formal evaluation of these mental health professional attachments in the UK and Europe. Bower and Sibbald (2000) in a review of the role of mental health practitioners in primary care distinguish between what they call the "replacement model" where a mental health professional takes on direct responsibility for the care of a person in primary care and the "consultation-liaison model" where the role of the mental health professional is to support the primary care staff in treating

patients. They also draw a useful distinction between the direct effects that mental health professionals might have on patients with whom they had contact, including symptoms or consultation rates with general practitioners, and indirect effects where the work of the mental health professional is focused on the behaviour of general practitioners and others in the primary care team, with patients not being seen by the mental health professional. Bower and Sibbald's review concentrated on the mental health "replacement model" and concluded that the impact on patient outcomes was modest, inconsistent and of limited duration, with the most impact on reduced consultation with family doctors and less prescribing of psychotropic drugs. Cape and colleagues (2007) conducted a similar but more extensive review than that of Bower and Sibbald (2000) comprising a total of 28 studies involving 3724 patients and also concluded that the overall effects on symptomatology were modest (standardised mean difference [SMD] -0.27, 95% confidence interval [CI] -0.34 to -0.21). It is interesting to note that of the 28 studies included in the Cape and colleagues (2007) review only four were conducted in the US, with 23 in the UK and one in Holland. As will be seen from the discussion below, this distribution is almost reversed when considering studies of collaborative care.

It could therefore be argued that two parallel tracks have developed in an attempt to improve the outcomes for people with common mental health problems in primary care: a British/European model, which has focused on the use of attached mental health professionals and has addressed anxiety disorders as well as depressive disorders, and an American model, which has focused on the development of a chronic care (collaborative care) model primarily for depressive disorders (some more recent collaborative care studies have looked at anxiety [Roy-Byrne *et al.*, 2005] and bipolar disorder [Simon *et al.*, 2005]). The question, then, is whether they represent substantially different approaches with the possibility of significantly different outcomes or whether they represent responses that are appropriate to the characteristics of the healthcare systems from which they have originated and will achieve broadly similar outcomes. For the purpose of this thesis the term *enhanced care* will be used to refer to any intervention designed to improve the delivery of care for depression in primary care. As such, the term covers both the *attached professional model*, where a professional directly provides care to patients, and the *collaborative care model*, where

the professional(s) is involved not only in the direct delivery of care but its coordination and monitoring.

Before discussing in detail the evidence for the effectiveness of the collaborative care model for depression, one further aspect of the organisation of mental health services that has implications for any enhanced care model for depression—the stepped care model—will be briefly discussed. Stepped care is a system of delivering and monitoring treatments so that the most effective yet least burdensome treatment is delivered to patients first (Davison, 2000). Such systems seek to enhance the efficiency of service delivery by providing low-intensity "minimal interventions" to a proportion of patients in the first instance, before providing more intensive treatments to those who do not improve with the first step (Bower & Gilbody, 2005). The most usual minimal interventions are those that are less dependent on the availability of professional staff and focus on patient-initiated approaches to treatment. These may include self-help materials such as books (Cuijpers, 1997) and computer programmes (Proudfoot *et al.*, 2004). The use of these materials may be entirely patient managed, which is often referred to as pure self-help, or involve some limited input from a professional or para-professional, which is often referred to as guided self-help (Goldberg *et al.*, 2004). Escalating levels of response to the complexity or severity of the disorder are often implicit in the organisation and delivery of many healthcare interventions, but a stepped care system is an explicit attempt to formalise the delivery and monitoring of patient flows through the system.

In the field of mental health in the UK, stepped care models are currently popular and underpin the organisation and delivery of care in a number of recent NICE mental health guidelines (see for example the guidelines for depression [NICE, 2004a] and anxiety [NICE, 2004b]). However, despite this current enthusiasm, the model is not supported by a strong evidence base. Bower and Gilbody (2005) reviewed the evidence for the use of stepped care in the provision of psychological therapies and were unable to find a significant body of evidence to support its widespread adoption. They set out three assumptions on which they argue a stepped care framework is built and which need to be considered in any evaluation of stepped care. These assumptions concern the equivalence of clinical outcomes (between minimal and more intensive interventions at

least for some patients), the efficient use of resources (including healthcare resources outside the immediate provision of stepped care) and the acceptability of minimal interventions (to both patients and professionals). They reviewed the existing evidence for stepped care against these three assumptions and found some limited evidence to suggest that stepped care might be a clinically and cost-effective system for the delivery of psychological therapies but no evidence that strongly supports the overall effectiveness of the model. Some evidence for the equivalence of minimal interventions comes, for example, from work on computerised cognitive behavioural therapy (Proudfoot *et al.*, 2004) and the use of written materials (Cuijpers, 1997). For the efficiency assumption, evidence is more difficult to identify, although there is some suggestion that computerised cognitive behavioural therapy may be more cost effective as therapist-delivered care (Kalenthaler *et al.*, 2002). Other evidence suggests that individuals in stepped care programmes may seek treatment in addition to the minimal interventions offered in the study and thereby undermine the efficiency assumption (Treasure *et al.*, 1996; Thiels *et al.*, 1998). More problems emerge when the acceptability assumption is considered; with some suggestion that stepped care models may be associated with lower rates of entry into studies (Marks *et al.*, 2003; Whitfield *et al.*, 2001). Bower and Gilbody (2005) suggest that some of these problems could be addressed by taking into account patient choice (possibly by offering a choice from a range of minimal interventions) and also by adjusting the entry level into the stepped care system to take account of the severity of the disorder. Past experience of treatment or treatment failure may also be a useful indicator of which level a patient should be entered into the stepped care model.

Since the publication of the Bower and Gilbody (2005) review, a study of stepped care for over 720 patients by Van Straten and colleagues (2006) has been published; this compared two forms of stepped care with a "matched care" control. Both forms of stepped care involved assignment to a psychological therapy, brief behaviour therapy (BT) with a strong self-help component and therapist-delivered CBT. The matched care control involved patients being allocated to an appropriate psychological treatment as determined by the responsible clinician, unlike the other two arms of the trial where the type and duration of treatment was determined by the trial protocol. Patients in the matched control received more treatment sessions but outcomes were no better than for

those patients in the other two arms. Although the study lacked power to determine whether the difference was statistically significant (despite including over 700 patients), it is possible that the two stepped care models were more cost effective (Hakkaart-van Rooijen *et al.*, 2006). However, both stepped care arms had higher attrition rates and there was some diversion, especially in the BT group, into additional treatments other than those delivered in the study. Outside of the area of psychological therapies a number of trials of collaborative care (for example, Hunkeler *et al.*, 2006) have included an element of stepped care; these are reviewed in the evaluation of collaborative care below.

### 2.7 The development of the collaborative care model for depression

As was discussed above, the development a collaborative care approach to the treatment of depression arose from a number of concerns, principal among them was the recognition that current care for depression was inadequate (Katon *et al.*, 1995), outcomes were poor (Wells *et al.*, 1994) and that costs of care were high, even when physical healthcare considerations were taken into account (Simon *et al.*, 1995). In addition, early attempts to implement treatment guidelines for depression proved inadequate (for example, Katon *et al.*, 1992). The model of collaborative care for depression both built on and contributed to the framework set out by Von Korff and colleagues (1997) and Kilbourne and colleagues (2004) set out above. The past 10 years have seen significant developments of the model; in many of the earlier studies of collaborative care, mental health professionals (in the initial stages these were psychiatrists and psychologists) provided the increased input, with the initial emphasis being on the coordination of care delivered by others (including practice nurses and GPs), and later the emphasis switched to a more direct responsibility of the mental health professional in undertaking a care-coordination role (often referred to as a case manager) (Katon *et al.*, 1995; Katon *et al.*, 1996; Unutzer *et al.*, 2002). More recently, others, including primary care nurses (Hunkeler *et al.*, 2000; Mann *et al.*, 1998; Rost *et al.*, 2001) or graduates without core mental health professional training (Katzelnick *et al.*, 2000; Simon *et al.*, 2000), have taken on this coordination role.

## 2.8 The effectiveness of the collaborative care model for depression

As the programmes for collaborative care of depression developed, so the link with the chronic care model became more explicit; the central argument being that depression is a chronic condition that shares many of the characteristics of other chronic diseases such as diabetes and heart disease (Wagner *et al.*, 1996). In depression, the term collaborative care is used almost universally to describe chronic care interventions and this is the term that will be used throughout the rest of this thesis. The large majority of collaborative care studies in mental health focus on depression (this is in contrast to the attached professional literature where there is a greater proportion of studies on anxiety disorders); reference will be made to the collaborative care studies of other disorders where appropriate.

The assessment of the impact of collaborative care for depression is complicated by the fact that, in contrast to efficacy trials of particular interventions, entry to the studies is often not as stringent. In efficacy trials of the pharmacological or psychological treatment of depression, typically patients would be included if they met criteria for major depression but excluded if they met criteria for minor depression or dysthymia. Similarly, cases of mixed anxiety and depression would be entered into a study only if there was an established diagnosis of depression. Moreover, patients already receiving treatment (usually medication) would often be excluded from many efficacy trials. However, in many trials of collaborative care this is not the case; for example, patients with dysthymia or mixed anxiety states may also be admitted to trials, and perhaps up to 50% of participants have already been prescribed antidepressants (for example, Hunkeler *et al.*, 2006; Wells *et al.*, 2000). This introduces some caution into the interpretation of the data on the collaborative care of depression.

A number of recent meta-analyses of collaborative care have supported the statistical and clinical effectiveness of the model for depression (Badamgarav *et al.*, 2003; Neumeyer-Gromen *et al.*, 2004; Gilbody *et al.*, 2006a; Cape *et al.*, 2007) but not necessarily the cost effectiveness (Ofman *et al.*, 2004; Gilbody *et al.*, 2006b). Other related reviews have focused on the use of case management in depression (Gensichen *et al.*, 2006), which they defined as "an intervention for continuity of care including at least the systematic monitoring of symptoms. Further elements were possible as

coordination and assessment of treatment and arrangement of referrals". Given this rather broad definition, the paper by Gensichen and colleagues (2006) was excluded from consideration in the review that follows.

The effect sizes on depressive and related symptoms described by the Badamgarav and colleagues (2003), Neumeyer-Gromen and colleagues (2004), Gilbody and colleagues (2006a) and Cape and colleagues (2007) reviews were modest, ranging between 0.25 (95% CI 0.18, 0.32) (Gilbody *et al.*, 2006a) and 0.75 (95% CI 0.70, 0.81) (Neumeyer-Gromen *et al.*, 2004), with most reviews reporting effect sizes at the lower end of the range indicated. The review by Cape and colleagues (2007) is the most comprehensive yet, including 29 separate studies of collaborative care from a total of 64 studies of the enhanced care of depression (and including some studies of dysthymia and anxiety). The review is important for a number of reasons: first, it places the work on collaborative care in a wider context and usefully allows for a comparison of the effect of collaborative care with other elements of the enhanced care of depression in primary care, including the effectiveness of the attached professional model (Bower & Sibbald, 2000); secondly, it includes a review of the type and intensity of interventions offered in collaborative care; thirdly, it also includes a consideration of the impact on the delivery of enhanced care by different professional groups including psychiatrists, depression care specialists and non-professionally qualified staff; and finally, it allows for a consideration of the healthcare system in which the interventions were provided. All of these factors are potentially important in determining the shape and content of an NHS-based model of collaborative care. Each of these four different aspects of the evaluation of enhanced care is now considered in turn.

**Collaborative care versus attached professional**

In the first comparison drawn from Cape and colleagues (2007), the average effect size on symptomatology for an attached mental health professional was 0.27 (SMD, 95% CI 0.21, 0.34) and for collaborative care involving similar mental health professionals was 0.29 (SMD, 95% CI 0.23, 0.34). Given the similarity of effect sizes and the closely overlapping confidence intervals it seems reasonable to conclude, at least initially in the absence of any direct comparisons, that there may be few if any differences in outcomes

between these two modes of delivery of care. When attempting to understand these results a number of factors need to be considered:

1. There is considerable variation in the nature of the collaborative care provided – in some cases it involved case managers taking on the long-term care of people with depression (for example, Simon *et al.*, 2004), in others it involved little more than advice and consultation with a psychiatrist (for example, Katon *et al.*, 1995).

2. There may be differences in the nature of the intervention provided; for example, within the attached professional model the professionals more consistently provided specific psychological interventions (for example, Scott *et al.*, 1997; Ward *et al.*, 2000) and this may have an impact on the effectiveness of the intervention. Some support for this comes from an analysis of the data reviewed by Cape and colleagues (2007), focusing on only depressive disorders, which produced broadly similar effect sizes to that for the overall analysis (attached professional 0.27 (SMD, 95% CI 0.18, 0.35), collaborative care 0.30 (SMD, 95% CI 0.24, 0.36).

3. It may be that the populations included in the trials were different (see the point above about diagnostic differences in trial populations) with the collaborative care studies tending to focus more on depressive disorders. (In the re-analysis of the Cape and colleagues (2007) in point (2) above the 17 included studies of attached mental health professionals used were drawn from a total data set of 30 studies, whereas the 13 included studies looking at collaborative care were drawn from a data set of 15 studies [collaborative care studies make more use of non-mental health professionals and para-professionals])

4. The issues of the comparators and the nature of the healthcare system in which the interventions were delivered should also be considered. For example, the majority of the attached professional studies were based in the UK (26 out of 30) and most of the collaborative care was based in the US (24 out of 29).

**The type and intensity of interventions**

These vary considerably across the trials of collaborative care. The early studies, for example Katon and colleagues (1992) usually involved a limited input where a

psychiatrist assessed the patient and then provided advice and training to the general practitioner. Later studies, such as that of Hunkeler and colleagues (2006), involved a more complex intervention including case managers and a number of expert physicians. What is clear is that no simple or obvious pattern of the relationship of effect size to the increased complexity of the components of collaborative care emerges from the review (further consideration of this is given in the discussion of the regression studies of collaborative care discussed below). In contrast, looking at the outcomes for the different types of attached professionals, a somewhat clearer picture emerges. For example, an attached professional providing a formal psychological treatment produces SMDs of 0.34 (95% CI -0.46, -0.23) for CBT and 0.29 (95% CI -0.44, -0.14) for counselling but only 0.09 (95% CI -0.30, -0.12) if the professional (in this analysis a psychiatric nurse) is simply focused on the coordination of care (Cape *et al.*, 2007). One possible interpretation of these results is that the provision of formal psychological treatment in primary care may have some advantages in the UK context over the simple coordination of care and that in the UK context collaborative care potentially adds less than in the US; however in the absence of direct comparisons, this remains speculative.

**The professional providing the enhanced care**

As already noted in the above section, the provision of coordination of services alone by a mental health professional (that is, not involving active treatment of individual patients) may have relatively little benefit. However, if the focus is on those professionals providing collaborative care, potentially important differences between professional groups emerge. SMDs differ between those interventions delivered by mental health specialists (including psychologists and specialist mental health nurses) (-0.29 [95% CI -0.48, -0.12]), psychiatrists (-0.32 [95% CI -0.51, -0.12]) and specifically trained graduate workers (-0.25 [95% CI -0.37. -0.13]) all of whom seem to be more effective than practice nurses (-0.15 [95% CI -0.23, -0.07]) or pharmacists (-0.14 [95% CI -0.23, -0.07]) (Cape *et al.*, 2007). Possible explanations for this may relate to the nature of the interactions between the professionals and the patients (including the development of a therapeutic relationship), the role taken on by the professionals in relation to others in the system or the approach taken by the existing staff in relation to the various professional groups. It is interesting to note that seven out of ten of the practice nurse studies and three out of four of the pharmacist studies took place in the

US (Cape *et al.*, 2007). This suggests that even if the studies were conducted in the US the impact of practice nurses or pharmacists is likely to be of limited clinical benefit and probably not cost effective.

**The nature of the healthcare system and the comparators used**

Forty seven per cent (14 out of 30) of the attached professional studies in the Cape and colleagues (2007) review, for example, had some form of active comparator, often another psychological intervention or medication. In contrast, only 28% (8 out of 29) of the collaborative care studies had an active comparator. However, there is a possibility that the nature of care proved in the "treatment as usual" arm may have involved significant interventions. In terms of healthcare systems, it is interesting to note that most collaborative care studies took place in the US, whereas most studies of an attached professional took place in Europe. Of the total of 29 studies of collaborative care identified by Cape and colleagues (2007), 26 were conducted in the US. Only five were conducted in Europe, three in the UK and two in Holland. The UK studies (Wilkinson *et al.*, 1993; Mann *et al.*, 1998 [two studies]) used practice nurses (that is, non-mental-health specialists) and showed no benefit. The two Dutch studies (Smit *et al.*, 2006; Brook *et al.*, 2003), a multifaceted collaborative care model and pharmacists supporting antidepressant use respectively, also showed no benefit.

As can be seen from the detailed consideration of the Cape and colleagues' (2007) review above, a number of factors in addition to the difference in healthcare systems could account for the differences in outcome, including the components of the collaborative care intervention, the nature of the treatment provided and the populations served. The possible differences between healthcare systems in the effectiveness of collaborative care may have something in common with the position of assertive community treatment or crisis response teams (see Chapter 1), in that a complex healthcare intervention is being advocated on the basis of international evidence, largely North American in origin, when UK and European studies are less positive. (However, it should be noted that one study of collaborative care for depression [Araya *et al.*, 2003] was excluded from the Cape and colleagues review as it was conducted in a developing healthcare system [Chile], and this produced a positive result). However, the fact that British and European studies do not consistently report the modest effects of

American studies would suggest that the statement by Simon (2006) that collaborative care models for depression should be widely adopted may be premature, at least for the NHS, and further evaluation is needed.

### 2.9 The effective components of collaborative care for depression

The key elements of collaborative care identified by Von Korff and colleagues (1997) emphasised the collaborative definition of problems, a problem-focused approach, and the provision of active and sustained follow-up to support the implementation of the care plan. Kilbourne and colleagues (2004), when considering the challenge of implementing collaborative care, emphasised the importance of leadership, decision support, delivery system design and clinical information systems. Collaborative care for depression has developed significantly over the past 15 years but few studies could be said to have fully met all the criteria set out by Von Korff and colleagues (1997) and Kilbourne and colleagues (2004). For example, in the study by Katon and colleagues (1995) collaborative care consisted largely of assessing patients and providing antidepressant medication, whereas in the study by Hunkeler and colleagues (2006) it consisted of a team-delivered programme of care including coordination by a depression care manager and the regular involvement of the primary physician, a psychiatrist, and a liaison primary care doctor. Treatment options included medication, behavioural activation, relapse prevention and problem solving therapy, and all were delivered within a stepped care framework.

Given the considerable variation in populations treated, interventions delivered and comparators, it is difficult to identify what the effective components of collaborative care may be. Indeed, if the views of Hawe and colleagues (2004) are considered, the application of the collaborative care model to the UK health services developed in the US should be based on the effective functions or elements of collaborative care and not a simple direct replication of all aspects of the programme. Such functions or elements have been identified by Von Korff and colleagues (1997) and Kilbourne and colleagues (2004) among others. The evidence for the effectiveness of these component elements will now be reviewed.

There are a number of possible approaches to identify the effective components of collaborative care. These include "de-construction" studies, akin to that of Jacobson and

colleagues (1996), which attempted a de-construction of the active elements of CBT. Unfortunately no relevant studies have been conducted in the area of collaborative care and the trend has been to add further elements to the care provided (for example, Hunkeler *et al.*, 2006). An alternative is to use regression techniques to examine existing studies and see if this can help to identify those potentially important functions or elements of collaborative care associated with positive changes.

Two systematic reviews of collaborative care, Bower and colleagues (2006) and Gilbody and colleagues (2006a), report on the use of meta-regression techniques to identify the potentially important components of collaborative care for depression. The studies were broadly similar in method and drew largely on the same set of studies of collaborative care in depression. Both explored a number of variables concerned with the provision of collaborative care that may be associated with a positive outcome. These included: the setting (that is, country) in which the treatment was delivered; the methods for identification of patients; the nature of the depressive disorder; the degree of training for primary care staff; the use of antidepressant medication and the strategies used for medication management; the provision of psychological treatment; the role and qualifications of the individual responsible for the coordination of care; the nature of the supervision made available to the collaborative care staff/team; and the frequency and duration of contacts. Neither review was able to analyse all these variables as it was not possible to extract from the relevant trial reports all the data required.

Bower and colleagues (2006) found that collaborative care had no impact on antidepressant adherence and that no other variables in the analysis were associated with antidepressant use (this was focused on because it is often a major objective of collaborative care). However, systematic methods for the recruitment of individuals, case coordinators with a mental health background, and the provision of regular supervision for case coordinators predicted positive outcomes on depressive symptoms. The analysis by Gilbody and colleagues (2006a) largely confirmed that of Bower and colleagues (2006). However, Gilbody and colleagues (2006a) focused on medication compliance and its relationship to outcomes, not whether collaborative care improved medication compliance *per se*. In their review they identified medication compliance as predictive of a positive outcome on depressive symptoms. They also identified the

professional background of the case coordinator and the use of effective supervision as predictive of a positive outcome on depressive symptoms, much in line with the conclusions of Bower and colleagues (2006). Interestingly, Gilbody and colleagues (2006a) found no greater benefit was gained from the addition of a psychological therapy to medication in collaborative care nor were an increased number of contacts with collaborative care staff associated with increase benefits. While a common set of results emerges from both of these reviews, they should be treated with caution as they are essentially observational data and do not allow for the kind of causal inferences that it may be possible to draw from an RCT. In addition, both Gilbody and colleagues (2006a) and Bower and colleagues (2006) acknowledge that there may be other important elements of the interventions that it was not possible to capture in the analysis through lack of available data and also because some elements of the interventions do not lend themselves easily to disaggregation. Nevertheless, both analyses provide important pointers to the identification of the key elements of a collaborative care intervention.

### 2.10 Summary: the effectiveness of collaborative care

A number of reviews of collaborative care have established that it produces consistent and significantly better outcomes both for a range of chronic diseases such as diabetes or heart disease (McAlister *et al.*, 2001) and for depression (Gilbody *et al.*, 2006a; Cape *et al.*, 2007). However, for depression the magnitude of the effect size is modest, around 0.25 (Badamgarav *et al.*, 2003; Neumeyer-Gromen *et al.*, 2004; Gilbody *et al.*, 2006a; Cape *et al.*, 2007), which is equivalent to about a 2-point change on the Beck Depression Inventory (BDI-II) or the Hamilton Rating Scale for Depression (HRSD). Changes of this magnitude raise questions about the clinical significance and cost effectiveness of the intervention; for example, the NICE guideline on the management of depression (Goldberg *et al.*, 2005) set a difference of 3 points on either the BDI-II or the HRSD for clinical significance, which is equivalent to an effect size of approximately 0.40. This would suggest that Simon's (2006) promotion of the widespread adoption of collaborative care may be premature. In addition, the understanding of the effective elements of collaborative care of depression is limited, with suggestions from regression studies that antidepressants, case management, mental health background and the supervision of case managers are important. However,

questions about the transferability of the intervention, and which of the key elements to preserve, remain given the variability in the comparators reported in the trials. The data-set on collaborative care also has little to say about the value of the intervention for patients with different levels and chronicity of depression, although trials suggest that patients with at least moderate depression (Gilbody *et al.*, 2006a) do well in collaborative care studies. The US trials also strongly emphasise the role of the case manager but, in contrast to collaborative care studies of chronic physical health problems, do not stress so much the development of self-help or related strategies. This would suggest that a careful examination of the effects of the key elements of collaborative care, such as the efficacy of antidepressants, the appropriate psychological treatment (which is not emphasised in many collaborative care trials) and the qualification and skills of the staff required to provide them should be considered, and this forms the basis of the next three chapters.

### 2.11 The limitations of this review

This review of collaborative care has a number of significant limitations. First, it relied on existing systematic reviews and did not involve a systematic review of primary studies; it is therefore possible that studies that would have had a direct bearing on the development of a UK-based evaluation of collaborative care have been not been identified (although the search strategies of the included reviews would not suggest this). In addition, both the reviews and the primary studies which formed the basis of the reviews contained little detail that might inform the development of a UK-based evaluation of collaborative care. In particular the detail on the nature, provision and uptake of psychological therapies was often missing or very limited. This deficiency will be addressed in the next three chapters which review the evidence for pharmacological interventions, psychological interventions and the competence required to deliver effective psychological interventions. The different populations including in the trials and developing nature of collaborative care also limited the conclusions that could be drawn as there was no consistent increase or decrease in average effect size over time (Gilbody *et al.*, 2006a).

The review concentrated on the clinical effectiveness of the interventions as established by the systematic reviews but found little about the important issues of clinical

significance or cost effectiveness, again because these issues were not covered by the original reviews. In addition, important data on other outcomes such as quality of life or satisfaction were excluded from the original reviews. This review was also limited in its consideration of organisational change, which again limits its capacity to inform the development of a collaborative care intervention in the UK.

The two reviews (Bower *et al.*, 2006; Gilbody *et al.*, 2006a) that used meta-regression techniques provided some information on what might be associated with positive outcomes in collaborative care but in the absence of formal testing of these elements of the programme it is not possible to be certain of their contribution to the outcomes of collaborative care. The reviews also say little about the impact of collaborative care on depression of varying severity and chronicity – an important consideration when the cost effectiveness of the intervention is uncertain and one which is addressed in the following three chapters. In significant part this is a function of the limited data provided in the trial reports but without direct comparisons of depression of different severity or chronicity, or possibly individual patient meta-analysis from the original trial data sets, it is unlikely that this problem could be addressed by existing reviews. Finally the lack of a substantial UK or European data set limits the conclusions that can be drawn about the potential effectiveness of the collaborative care mode in the UK

# 3. The Efficacy of Pharmacological Interventions (Selective Serotonin Reuptake Inhibitors) in the Treatment of Depression

## 3.1 Introduction

Antidepressants are widely accepted as the primary method for the treatment of depression in the UK and prescriptions for them have risen steadily over recent years. In the UK in 2005 a total of 29.3 million prescriptions were issued and represented a total spend of £292.2 million (www.ppa.org.uk). Antidepressants form a central part of most collaborative care interventions and Gilbody and colleagues (2006a) have demonstrated, in a meta-regression of collaborative care studies, an association between their use and positive outcomes. However, controversy still surrounds their efficacy in routine care; there are questions about whether they produce a clinically significant benefit over placebo (Moncrieff & Kirsch, 2005) and about their risk/benefit ratio for depression of varying severities (Goldberg *et al.*, 2005). Addressing these questions in regard to developing the role of antidepressants in the treatment of depression as part of a collaborative care programme is the primary focus of this chapter.

Antidepressants were first introduced into clinical practice in the 1950s and included the monoamine oxidase inhibitors (MAOIs) and the tricyclic antidepressants (TCAs). In much current antidepressant prescribing for depression[3] these drugs have been supplanted by the selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine and paroxetine, and more recently the so-called "dual action" drugs, such as the serotonin and noradrenaline reuptake inhibitors (SNRIs), for example venlafaxine. The relatively better side-effect profile and generally increased safety in overdose has seen the SSRIs recommended as first-line treatment in many clinical guidelines (for example, APA, 2000; NICE, 2004a). Together the SSRIs and SNRIs now account for over 60% of all antidepressant prescribing in the UK (www.ppa.org.uk).

Over the past 40 years many reviews have been conducted of the efficacy of all the antidepressants including recent well-conducted reviews such as those by Anderson and colleagues (2000), Geddes and colleagues (2000b) and Bauer and colleagues (2002a &

[3] Note that antidepressants including TCAs (such as amitriptyline) are used for other disorders such as atypical facial pain (McQuay *et al.*, 1996).

b), while others have looked at particular antidepressants such as amitriptyline (for example, Barbui & Hotopf [2001]). The purpose of this chapter is not to summarise all of these reviews, but, as stated above, to consider the efficacy of the most widely used of the current antidepressants, the SSRIs, in relation to the development of a collaborative care intervention and focusing on two important aspects of the use of antidepressants: their efficacy against placebo and their relative efficacy for depression of differing severities. Other factors including adherence to treatment, and interventions to support adherence and maintenance treatment, will also be considered.

### 3.2 Methodological concerns in assessing the efficacy of antidepressants

The methodological problems associated with the use of RCTs have previously been reviewed in Chapter 1 and will not be rehearsed again, but some specific issues relating to the evaluation of antidepressants, including the placebo effect and spontaneous recovery, are considered below.

#### The placebo effect

The main comparator in most efficacy trials of SSRIs is an inert placebo. (The use of active placebos, designed to mimic the side effects of antidepressants [Moncrieff *et al.*, 2001] has fallen from favour in recent years). Comparisons with placebo are important as some have argued that the placebo effect can in fact account for most, if not all, of the benefits obtained from antidepressants (Kirsch *et al.*, 2002a). For example, in two meta-analyses (Kirsch & Sapirstein, 1998; Kirsch *et al.*, 2002a) it has been argued that up to 80% of the effect of antidepressants can be explained by the placebo response. Although the earlier of these two meta-analysis was criticised because it included only a limited number of published trials, the later work analysed all data (including unpublished trials) submitted to the US Food and Drug Administration for the licensing of new antidepressants, including the SSRIs and venlafaxine.

A number of factors may contribute to the placebo effect, including simply being engaged in treatment (Andrews, 2001), the nature of the delivery of the intervention, the frequency and duration of any contacts associated with its delivery and the explanations given as to the potential benefits or disbenefits of taking the placebo (Salamone, 2000). Most commentators on the placebo effect attribute its power to expectancy effects (Kirsch *et al.*, 2002a). Some evidence for this in relation to antidepressants comes from

a meta-analysis by Posternak and Zimmerman (2007) who examined the impact of frequency of contact with clinicians during clinical trials of antidepressants and suggested that increased contact with a clinician during the course of a trial was associated with an increased placebo effect. Others have argued that classical conditioning may also play a part (Stewart-Williams and Podd, 2004).

There is some evidence to suggest that the placebo response is less marked as the severity of the depression increases (Angst, 1993; Khan *et al.*, 2002), with little clinical benefit being discernable in comparisons between SSRIs and placebo in mild depression (Kirsch *et al.*, 2002a). This presents particular problems in the interpretation of trials of antidepressants as in many cases there is a bias to the recruitment of people with less severe depression. The level of increased trial recruitment via media advertising (Greist *et al.*, 2002) and the reluctance of clinicians to enter severely ill patients into clinical trials when it is possible they will be given a placebo (Thase, 2002) are two factors influencing this potential bias. Further support for this view comes from a study by Walsh and colleagues (2002) who have suggested that the response rates to both placebo and active drugs are increasing at a rate of 7% per year. This further complicates the identification of possible beneficial effects of antidepressants because when placebo response rates exceed 40%, individual trials may lack the power to detect potential benefits (Thase, 2002) and meta-analysis will be required to detect any differences. Walsh and colleagues (2002) report a correlation ($r = +0.43$) between the extent of the placebo response and the year of trial publication and a similar but less robust association ($r = +0.26$) between extent of the response to antidepressants and the year of publication. Finally, there is some limited evidence to suggest that the placebo effect may not be as persistent as the drug effect, particularly in atypical depression (Quitkin *et al.*, 1987).

There is other evidence to suggest that the response to antidepressants is more than a simple placebo response. This includes data suggesting a reduction in the duration of depressive episodes of over 25% in treated as opposed to untreated depression (Solomon *et al.* 1997), an increased rate of relapse for those on placebo compared with those on antidepressants (Ross *et al.*, 2002), and a faster response to antidepressants than to placebos (Taylor *et al.*, 2006).

**Spontaneous recovery**

Another important aspect in the recovery from depression is spontaneous recovery, which is defined as the recovery from a disorder without any apparent external intervention. The issue of spontaneous recovery in depression is well reviewed by Posternak and colleagues (2006). The average course of an untreated depressive episode is between 6 and 8 months (Coryell *et al.*, 1995). Coryell and colleagues (1995) also suggest that much of the spontaneous response seen in a cohort of depressed people occurs in the first 3 months, with almost 85% recovered by 1year. There is evidence to suggest that patients who do not seek treatment for their depression may recover more quickly than those who seek but do not receive treatment (Posternak *et al.*, 2006). There is also some evidence to suggest that people who do not seek help have a shorter mean duration of depressive episode (Posternak *et al.*, 2006). Posternak and colleagues (2006) further argue that this relatively high spontaneous remission rate may explain why studies conducted in primary care aimed at increasing the detection of major depression (Coyne *et al.*, 1997; Schulberg *et al.*, 1987; Tiemens *et al.*, 1999), or using more intensive treatment (Koenig *et al.*, 1989; Schulberg *et al.*, 1996; Simon *et al.*, 1995), have often failed to demonstrate significantly improved outcomes compared with usual care. They also suggest that such studies should consider including only patients who have been depressed for a minimum of 3 months, since it is during this time that spontaneous remission is most likely to occur.

Posternak and colleagues (2006) provide an estimate of the percentage of subjects in controlled treatment trials who experience a spontaneous remission of symptoms. Drawing on their group's previous work (see Posternak & Miller, 2001), they estimate that if 50% of depressed individuals spontaneously recover within 6 months, this would give a spontaneous remission rate of depression of about 2% per week over 6 months. This corresponds to a recovery rate of between 12% and 16% in the average antidepressant 8-week trial, irrespective of whether participants were in the placebo or the antidepressant arm of the trial. Posternak and colleagues (2006) further argue that because remission of the disorder sets a higher threshold for improvement than response (defined in most trials as a 50% reduction in symptom severity—see below), the percentage of spontaneous responders may even be higher and may account for a significant number of responders in the placebo arm of a clinical trial.

**Trial populations**

A number of commentators have drawn attention to the problems of trial populations in antidepressant trials, including recruiting through public advertisement and the payment of patients for entry into trials (Greist *et al.*, 2002; Thase, 2002). In addition, the consensus is that clinicians are less likely to enter less severely depressed patients in trials and also to withdraw the more severely depressed patients as they become concerned that the patients may not be benefiting from treatment (Stassen *et al.*, 1993); this is despite the fact that there is more likely to be a true drug effect in people who are more severely depressed (Khan *et al.*, 2002).

**The type of depression**

There are a number of subtypes of major depression including, for example, melancholic depression (characterised by symptoms such as anhedonia, non-reactive mood, diurnal variation in mood and psychomotor disturbance), atypical depression (characterised by symptoms such as hyperphagia, hypersomnia and intense feelings of lethargy), treatment-resistant depression (defined as depression that has not responded to two adequate courses of an antidepressant) and psychotic depression (depression accompanied by psychotic features). However, there is little evidence linking the type of depression to successful treatment with a particular antidepressant or class of antidepressant (Anderson *et al.*, 2000). Some evidence suggests that MAOIs may be less effective than TCAs in hospitalised patients but more effective in non-hospitalised patients with atypical depression (Quitkin, 2002). There is also some limited evidence to suggest that TCAs may be more effective than SSRIs in depressed inpatients (Anderson *et al.*, 2000; Geddes *et al.*, 2000b) and that older adults may take longer to respond to antidepressant medication (Anderson *et al.*, 2000).

**Outcome measures**

The outcome measures used in clinical trials of antidepressants are subject to the same general criticisms of trial outcome measures raised in Chapter 1. However, two additional problems are often encountered in the reporting of antidepressant trials: the use of completer analyses and of a "percentage" improvement measure usually referred to as "response to treatment" or a "responder analysis".

Completer analyses that are used in the reporting of drug trials do not report the scores of participants who have dropped out before the end of the trial. As it is possible that participants who drop out or who are withdrawn from a study are more likely to have had a poor response, their exclusion is likely to bias the analysis to a more positive result. The solution to this problem is to adopt an "intention to treat" approach to data analysis and enter into the analysis the last measure obtained before the participant left the study (often referred to as "last observation carried forward"). Although this may also introduce bias into the analysis, such bias may be avoided by the use of more sophisticated analysis of the data (Beunckens *et al.*, 2005; Horton & Kleinman, 2007).

Of more importance is the use of "responder" data in the evaluation of drug trials. In this case, improvement on a continuous measure, for example the HDRS is in effect represented as a dichotomous measure by categorising as "responders" all patients who have experienced a reduction in their baseline scores of an agreed percentage (usually 50%). While this is apparently a simple way to deal with the fact that many people in trials experience incomplete recovery, it has considerable flaws. The major problem, which is well described by Kirsch and Moncrieff (2007), is that a small and probably non-clinically significant difference in means on a continuous measure between the two arms of a trial can turn into an apparently clinically and statistically significant difference when the data are transformed into dichotomous "responder" data.

**Side effects and other harms**

The assessment of the side effects of antidepressant medication is important for two main reasons; first because of the harm that may occur to any patient taking it and secondly because, even if transitory, they may reduce the likelihood of a patient adhering to a potentially beneficial treatment. Side effects of antidepressant use may include immediate (for example, nausea on initiation of treatment) and long-term effects (for example, weight gain) (Goldberg *et al.*, 2004). Side effects tend to be dose related and vary considerably in severity from transient nausea to a significant exacerbation in suicidal ideation. Unfortunately trials differ significantly in the degree to which they report side effects; sometimes they may be noted but not specified or they may be grouped under particular headings, for example gastrointestinal, neurological or cardiovascular. In published reports space limitations may preclude effective reporting

of side effects and rare but important events such as suicide may not be detected, particularly in short-term trials. Cardiovascular side effects are particularly important, given the high incidence of depression in people with cardiovascular disease. For example, Glassman and colleagues (2002) report a prevalence of major depression of approximately 20% in patients with coronary heart disease, while Carney and colleagues (1997) report a three to fourfold increase in cardiovascular morbidity and mortality in depressed people. Fortunately there is some evidence to suggest that the use of certain SSRIs such as sertraline or citalopram may contribute to an improvement in depressive symptoms and reduction in cardiovascular risk (Glassman *et al.*, 2002; Lesperance *et al.*, 2007). Conversely there is some evidence to suggest an increased risk of cardiovascular problems with the TCAs (Hippisley-Cox *et al.*, 2001) as compared with SSRIs (Roose, 2001; Goeringer *et al.*, 2000).

In addition to these side effects, two other related issues are of concern in the assessment of antidepressant medication: safety in overdose and withdrawal symptoms experienced on stopping medication. Again, and perhaps not surprisingly, these two issues are not reported on to a great extent in short-term trials, but they can be important in determining the choice of antidepressant. The major risk in overdose comes from the TCAs; antidepressants were involved in 18% of deaths from drug poisoning between 1993 and 2002 (Morgan *et al.*, 2004), with TCAs accounting for 89% of these cases. Discontinuation symptoms can occur on abrupt cessation of all classes of antidepressants and are more likely with some drugs (for example, paroxetine) but are usually mild and self-limiting (Lejoyeux *et al.*, 1996; Haddad, 2001). There has also been increasing concern that antidepressants may be associated with an increase in suicidal ideation (Jick *et al.*, 2004), but it is not clear whether this is the direct result of taking an antidepressant, or arises from the depression itself. The current consensus is that, while there may well be an increased risk of suicide associated with antidepressant use in children and adolescents (for example, Whittington *et al.*, 2004), this is less of a concern in adults (MHRA, 2004).

The absence of clear reporting of side effects often means that a crude proxy of the acceptability of the intervention has to be used and this is often the dropout rate from

trials. In some cases it may be indicated in the trial report whether dropout was due to side effects, but this is not always the case.

### 3.3 Review of the efficacy of SSRIs against placebo

This systematic review and meta-analysis compares the effectiveness of SSRIs with placebo. It considers first the evidence for the overall effectiveness of SSRIs in major depressive disorder and then reviews the effectiveness of SSRIs for depression of different severities.

#### Method

This review follows the methods outlined in established manuals in the field including those of NICE (2007), the Cochrane Collaboration (2003) and Egger and colleagues (2001). The criteria for evidence searching including the search filters and search strategy were first established, followed by a critical appraisal of the identified papers and finally the synthesis and meta-analysis of the extracted data from the trials. The review was led by the author in conjunction with a research fellow and a research assistant who participated in the joint evaluation of the studies and extraction of the data as required by the above methods. Expert advice from an academic psychopharmacologist and a psychiatric pharmacist was provided, including specific advice on appropriate doses of drugs and a review of study inclusion and exclusion criteria.

#### Development of the search filters

Search filters that combined subject headings with free-text phrases were developed to search relevant electronic databases. A filter was developed for the general topic "depression", which was combined with specific filters for SSRIs. These were also combined with filters developed for RCTs (Appendix A). The initial searches were undertaken in September 2002, with update searches being carried out until December 2004. The following databases were searched: EMBASE, MEDLINE, PsycINFO, Cochrane Library and CINAHL. In addition, hand searches were also made of the reference lists of all eligible RCTs.

**Study selection**

All references located in searches of electronic databases were downloaded into Reference Manager (ISI ResearchSoft, 2002) and searched by one reviewer to exclude irrelevant papers. The titles of excluded papers were double-checked by a second reviewer. All primary-level studies included after the first scan of citations were acquired in full and re-evaluated for eligibility. Trials were included if the patient population had an appropriate primary diagnosis of major depressive disorder (that is International Classification of Diseases [ICD-10; World Health Organisation, 1992], Diagnostic and Statistical Manual of Mental Disorders [DSM-IV; American Psychiatric Association, 1994], Research Diagnostic Criteria [Spitzer *et al.*, 1978] or Feighner criteria [Feighner *et al.*, 1972]) and the intervention was an SSRI. The following were excluded: trials of children and adolescents (defined as less than 18 years old); treatment options not routinely available in the NHS; trials with patients with significant comorbid medical illnesses or mental disorders; and trials where SSRIs were used in a primary preventative manner. All eligible papers were critically appraised for methodological quality (see Appendix B), which focused primarily on an assessment of the adequacy of the randomisation procedure and whether or not assignment to treatment groups was concealed as these two factors have been shown to be most associated with a reduction in bias (Schultz *et al.*, 1995).

In addition to the basic inclusion and exclusion criteria, a number of additional criteria concerning diagnosis were used to ensure uniformity of the trials reviewed. These are set out below:

- In trials where some participants had a diagnosis of bipolar disorder, at least 85% had to have a primary diagnosis of major depressive disorder and no more than 15% a diagnosis of bipolar disorder.
- In trials where some participants had a primary diagnosis of dysthymia, at least 80% of trial participants had to have a primary diagnosis of major depressive disorder, and no more than 20% a sole diagnosis of dysthymia.

To be included, studies also had to have, as a minimum, extractable data from the HRSD (any version) or Montgomery-Asberg Depression Rating Scale (MADRS) (see below) on the following outcomes:

- the number of participants who remitted (that is, achieved below the equivalent 17-item HRSD score of 8)
- the number of participants who responded (achieved at least a 50% reduction in scores)
- mean endpoint data
- at least 50% of the patients remaining in the trial at the end of the trial.

There is evidence that dosages of antidepressants below the agreed therapeutic dose produce suboptimal outcomes (Thompson & Thompson, 1989; Bollini *et al.*, 1999). In order to account for this, studies were included provided there was clear evidence that at least 75% of patients received the standard dose or the mean dose used was at least 105% of the standard dose. The standard dose was either that stated by Bollini *et al.* (1999) or, for drugs not included by Bollini and colleagues, the dose stated by the British National Formulary (BNF, 2003). This was because it was decided, on expert advice, that the standard doses for some drugs in the BNF, particularly drugs licensed some time ago, were too high.

In order to better understand the potential value of antidepressants in the provision of collaborative care, an analysis by setting was undertaken where possible. To facilitate this, studies were categorised by: (a) primary care (where this was specifically indicated); (b) inpatient (where at least 75% of the participants were initially treated as inpatients); and (c) secondary care (including outpatients where this was specifically indicated). However, data from these analyses should be treated with some caution, as the thresholds for entry into these settings are likely to vary across different healthcare systems.

### 3.4 Synthesising the evidence

#### Outcomes

Data were extracted for scores on two clinician-rated scales for depression, the HRSD and the MADRS, at the end of treatment and, where available, at follow-up. Both continuous (for example, mean endpoint scores) and dichotomised data (for example, number of people achieving below the cut-off for remission as defined by pre-

determined scores on the relevant scale) were used. As an important element of the review was to try and determine whether there were differences in response to antidepressants according to severity, the mean depression score at baseline (most commonly an HRSD score) was extracted and used as a proxy measure of severity. (Very few studies gave information about participants' baseline severity of depression according to standard diagnostic procedures). Scores were categorised mild, moderate, severe or very severe according to American Psychiatric Association criteria (American Psychiatric Association, 2000; see Appendix C). Where necessary, different versions of the HRSD were standardised using the method for pro-rating suggested by Walsh and colleagues (2002). These categories were used with caution, particularly given the variation in the standard deviation around baseline mean scores.

**Data extraction**

Outcome data from all eligible studies that met quality criteria were extracted using a standard extraction form (see Appendix D) and entered into Review Manager 4.2 (Cochrane Collaboration, 2003). For incomplete data, where possible the original authors were contacted and additional information was sought. If standard deviations were not provided in the trial reports, standard conversion formulas were used to calculate them (see Appendix E). All dichotomous outcomes were analysed on an intention-to-treat basis (that is, a "once-randomised-always-analyse" basis). This assumes that those participants whose outcomes were not reported – from whatever group – had an unfavourable outcome. All extracted data was checked by a second reviewer for accuracy and where any disagreement arose a third reviewer was consulted. Masked assessment (that is, blinding the reviewer to the journal title, the authors, the institution, or the magnitude of the effect) was not used since it is unclear that doing so reduces bias (Jadad *et al.*, 1996; Berlin, 1997).

**Meta-analysis**

Meta-analysis was used to synthesise data. Dichotomous outcomes were analysed as relative risks (RR) with 95% confidence intervals. A relative risk (or risk ratio) is the ratio of the treatment event rate to the control event rate. An RR of 1 indicates no difference between treatment and control. Continuous outcomes were analysed as standardised mean differences (SMD) (again with 95% confidence intervals) because

different versions of the scales were reported in trials and also because it was necessary to combine outcomes from both the HRSD and MADRS.

Heterogeneity was assessed using both the $I^2$ and the chi-squared tests of heterogeneity ($p < .10$), as well as visual inspection of the forest plots. The $I^2$ statistic describes the proportion of total variation in study estimates that is due to heterogeneity (Higgins & Thompson, 2002). An $I^2$ of less than 30% was taken to indicate mild heterogeneity and a fixed effects model was used to synthesise the results. This assumes that the underlying effect is the same (Egger *et al.*, 2001). An $I^2$ of more than 50% was taken as major heterogeneity. If this were the case, an attempt was made to explain the variation, such as different populations or interventions. If studies with heterogeneous results were found to be comparable, a random effects model was used to summarise the results (DerSimonian & Laird, 1986). In a random effects model, heterogeneity is accounted for both in the width of CIs and in the estimate of the treatment effect. An $I^2$ of 30% to 50% was taken to indicate moderate heterogeneity. In this case, both the chi-squared test of heterogeneity and a visual inspection of the forest plot were used to decide between a fixed and random effects model. Finally, to examine the possibility that the results suffered from publication bias, data from included studies were entered, where there were sufficient data, into a funnel plot. Asymmetry of the plot was taken to indicate possible publication bias and was investigated further.

**Assessing the clinical significance of the meta-analyses**

When attempting to determine the potential clinical significance of the results of the analyses, in addition to taking into account the trial population and nature of the outcome, two *a priori* indicators were used. These followed the conventions developed in NICE mental health clinical guidelines (for example, Kendall *et al.*, 2002; Elhers *et al.*, 2005) where for a dichotomous outcome an RR of 0.80 or less was considered clinically significant and for a continuous outcome an SMD (effect size) of approximately 0.5 (a 'medium' effect size [Cohen, 1988]) or higher was considered clinically significant.

### 3.5 Studies considered for review[4]

One hundred and three studies were found in a search of the electronic databases with 48 being included and 55 being excluded after assessment (see Appendix F). Six studies were of citalopram (BURKE02, FEIGHNER99, MENDELS1999, MONTGOMERY2001, MONTGOMERY92A, STAHL00); 17 of fluoxetine (ANDREOLI2002, BYERLEY88, COHN1985, COLEMAN01, DUNLOP1990, FEIGHNER89A, MCGRATH00, O'FLYNN1991, RICKELS1986, RUDOLPH99, SIL'STNE99, SRAMEK95, STARK85, THAKORE1995, VALDUCCI1992, WERNICKE1987, WERNICKE1988); 12 of fluvoxamine (CLAGHORN1996, CONTI1988, DOMINGUEZ85, FABRE1996, FEIGHNER1989, ITIL1983, KASPER95, LYDIARD1989, LAPIERRE1987, NORTON1984, ROTH90, WALCZAK1996); eight of paroxetine (CLAGHORN92A, EDWARDS93, FEIGHNER92, HACKETT1996, MILLER1989, RICKELS1989, RICKELS1992, SMITH1992) and five of sertraline (COLEMAN1999, CROFT1999, FABRE95, RAVINDRAM1995, REIMHERR90). These provided data for up to 7,460 trial participants.

All included studies were published between 1983 and 2003 and were between 4 and 24 weeks long (mean = 6.75 weeks), with 16 trials of 8 weeks or longer. Three studies were of inpatients, 31 of outpatients, one in primary care and 13 either mixed or unspecified. In no study were more than 80% of study participants aged 65 years and over. It was possible to determine baseline severity in 19 studies, with four being classified as moderate, six as severe and nine as very severe. Information about each study along with an assessment of methodological quality is in Appendix G, which also contains a list of excluded studies along with reasons for exclusions. Fifteen studies were excluded from all efficacy outcomes because more than 50% left treatment early (CLAGHORN1996, COHN1985, CONTI1988, DOMINGUEZ85, EDWARDS93,

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[4] Here and in Chapter 4, following the Cochrane convention, each study considered for review is referred to by a 'study ID' made up of first author and publication date in capital letters (unless a study is in press or only submitted for publication, when first author only is used). References for these studies are in Appendix F.

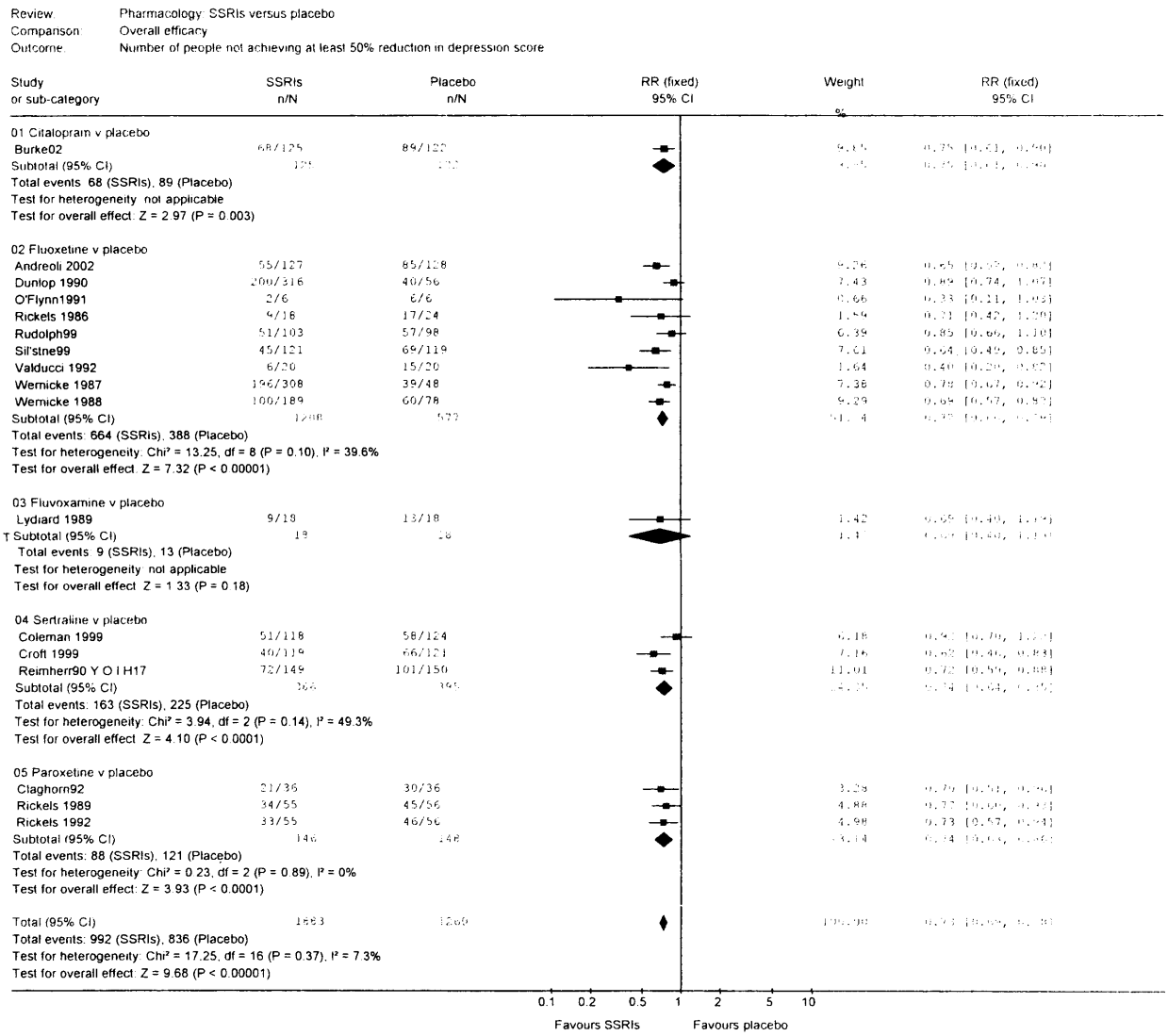
FABRE95, FABRE1996, FEIGHNER1989, FEIGHNER92, ITIL1983, LAPIERRE1987, SMITH1992, STAHL00, STARK85, WALZAK1996). Studies were also excluded from the sub-analyses of severity if mean baseline scores for depressive symptoms were not available. Visual inspection of funnel plots of the meta-analyses (see below) of the studies indicated the possibility of publication bias. This was confirmed by the MHRA report (MHRA, 2004), which revealed significant numbers of unpublished studies of all the SSRIs. This again introduces some caution into the interpretation of the results.

**Comparison 1[5]: SSRIs versus placebo – effect of treatment on efficacy outcomes**

The data on SSRIs versus placebo is presented in Figure 3.1. As can be seen from the forest plot, there is evidence of a clinically significant difference (a 50% reduction in depressive symptoms) in favour of SSRIs as measured by the HRSD (N = 17; n = 3143; RR = 0.73; 95% CI, 0.69 to 0.78).

[5] Here and in Chapter 4, 'N' refers to the number of trials and 'n' to the number of participants in each comparison.

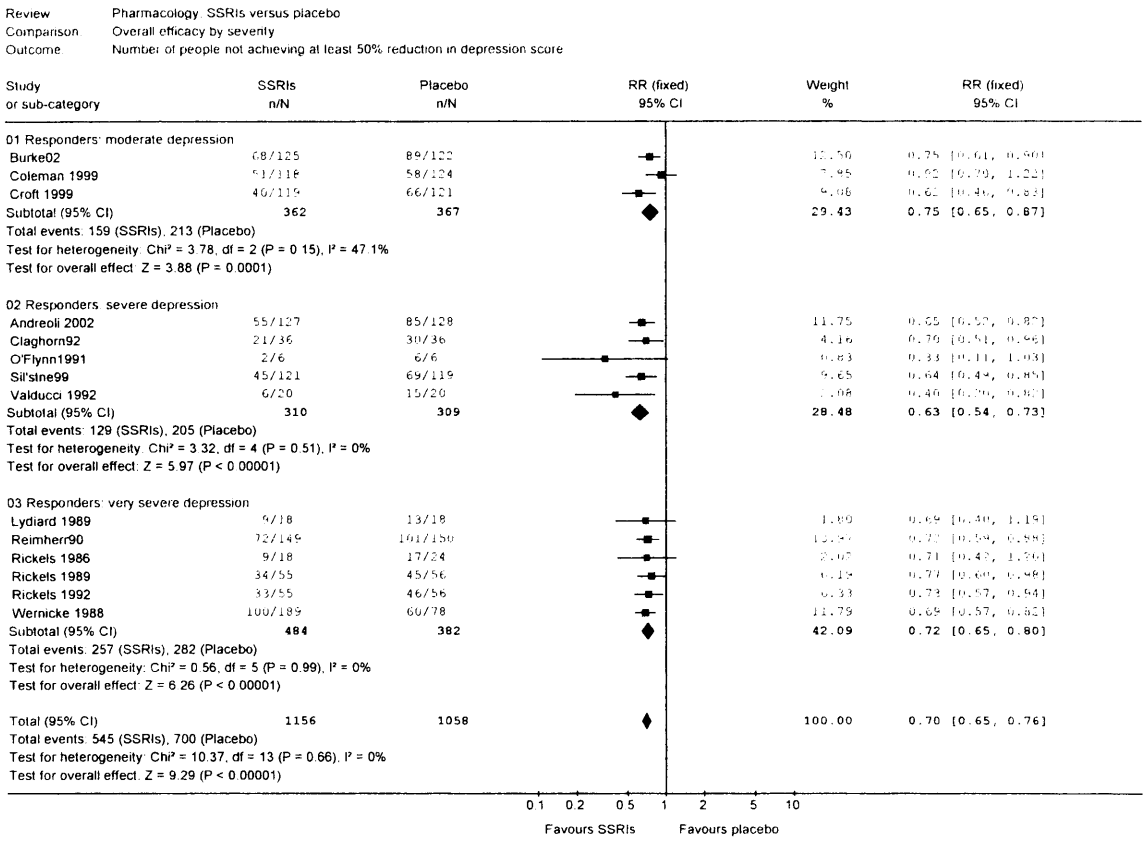
**Figure 3.1[6]: SSRIs versus placebo – 50% reduction in depression score**




The data presented in Figure 3.2 is also supportive of the relative benefit of a 50% reduction in depressive symptoms for SSRIs over placebo as measured by the HRSD for: moderate depression (N= 3; n= 729; RR= 0.75; 95% CI, 0.65 to 0.87); severe depression (N= 5; n= 619; RR= 0.63; 95% CI, 0.54 to 0.73); and very severe depression (N= 6; n= 866; RR= 0.72; 95% CI, 0.65 to 0.8).

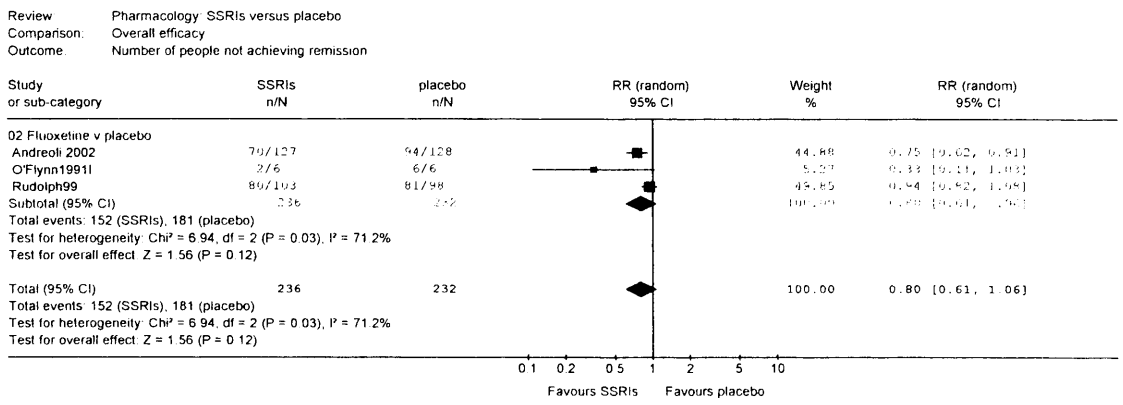
[6] Data are presented in forest plots in Chapter 3 and 4 to facilitate understanding of the data anlaysis. As a general rule forest plots are used to present data from the analysis of 3 or more studies, where 1 or 2 stu dies are meta-analysed the results are usually presented in the body of the text.

**Figure 3.2: SSRIs versus placebo: 50% reduction in depression score by severity**



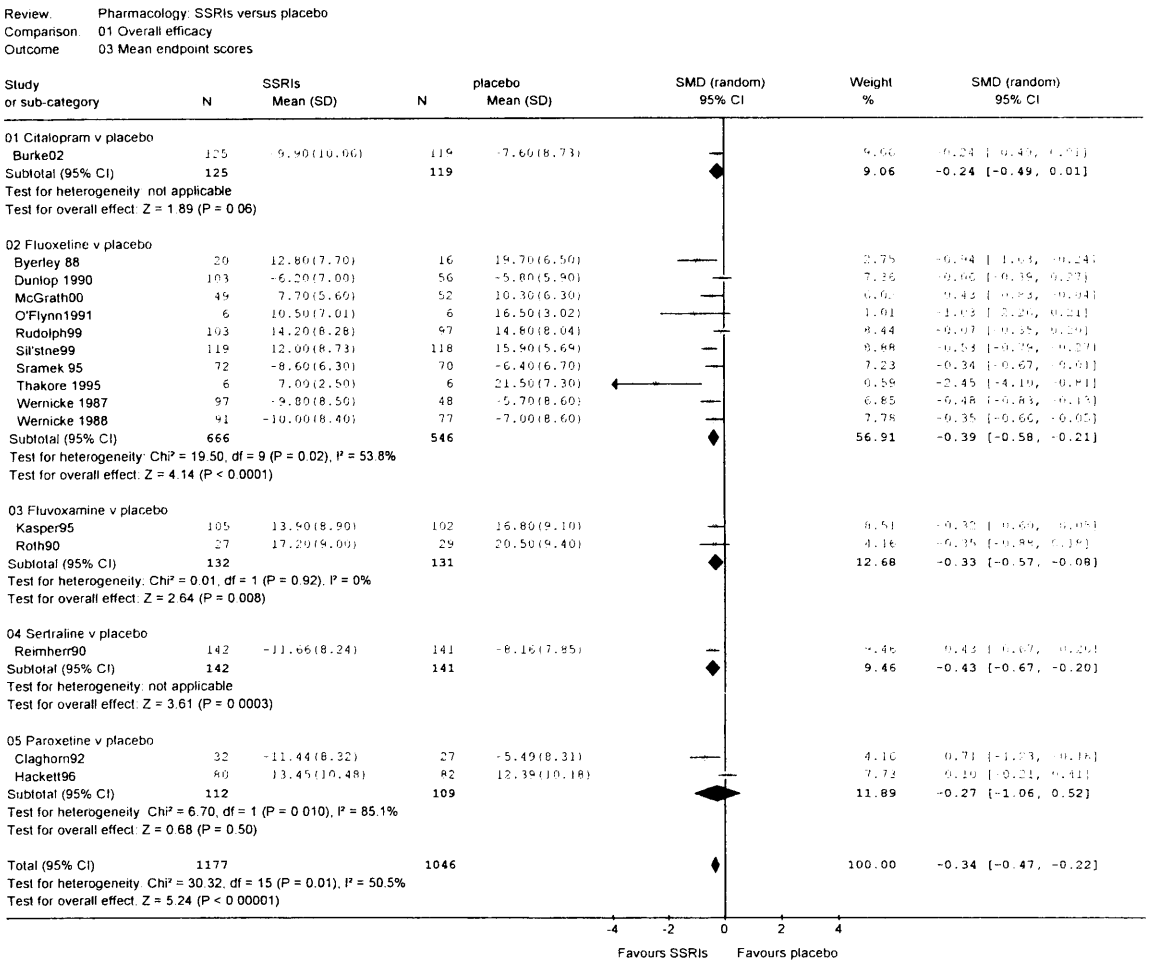

However, an examination of the data presented in Figure 3.3 shows that when the more stringent criteria of remission is used the results are not so convincing. In the overall comparison of SSRIs with placebo, although the relative risk approached what could be considered clinically important, the difference did not reach statistical significance as measured by the HRSD (N= 3; n= 468; RR [random effects] = 0.8; 95% CI, 0.61 to 1.06).

**Figure 3.3: SSRIs versus placebo: number not achieving remission**



When data on the continuous measures at the end of treatment are considered (see Figure 3.4) then the analysis, although reaching statistical significance, fails to meet the pre-determined level of SMD (0.5) for a clinically important difference as measured by the HRSD (N= 16; n= 2223; SMD [random effects] = -0.34; 95% CI, -0.47 to -0.22).

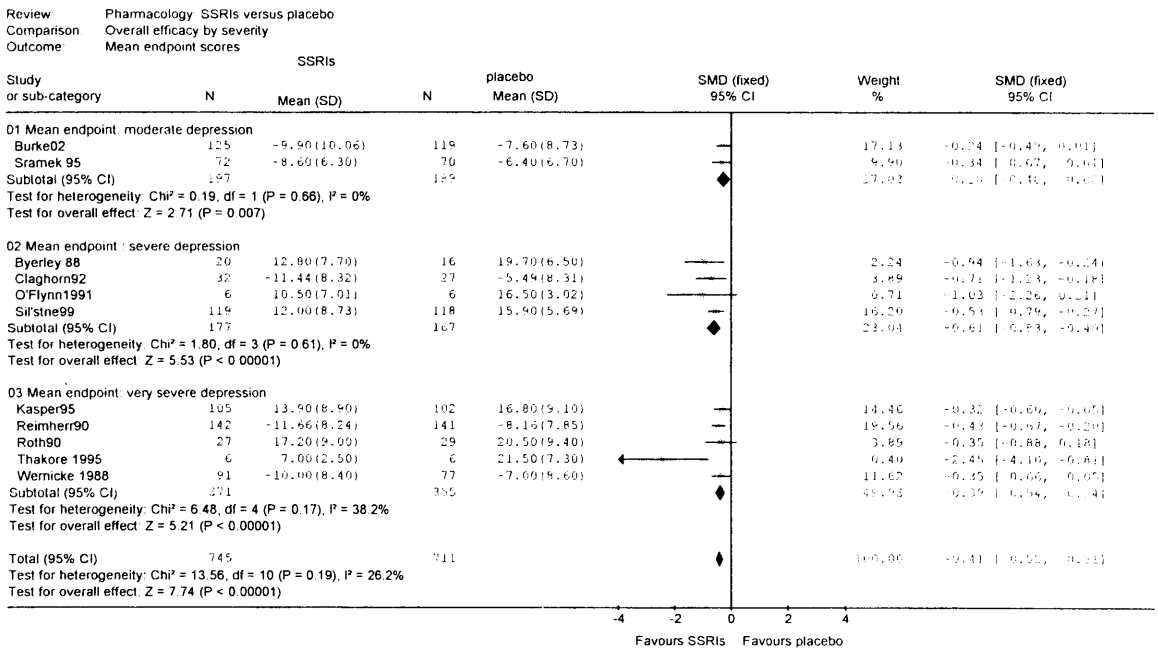
**Figure 3.4: SSRIs versus placebo: mean endpoint scores**




An analysis by severity produces a somewhat mixed picture (see Figure 3.5). For moderate depression there is evidence of a statistically significant difference favouring SSRIs on reducing depressive symptoms as measured by the HRSD at endpoint but the size of this difference is unlikely to be of clinical importance (N= 2; n= 386; SMD= -0.28; 95% CI, -0.48 to -0.08). The picture is more encouraging for severe depression, with the analysis favouring SSRIs over placebo on reducing depression symptoms as measured by the HRSD (N= 4; n= 344; SMD= -0.61; 95% CI, -0.83 to -0.4). However,

the pattern of increasing benefit with severity is reversed for very severe depression, where although the difference is statistically significant it is unlikely to be of clinical importance for depressive symptoms, as measured by the HRSD (N= 5; n= 726; SMD= -0.39; 95% CI, -0.54 to -0.24).

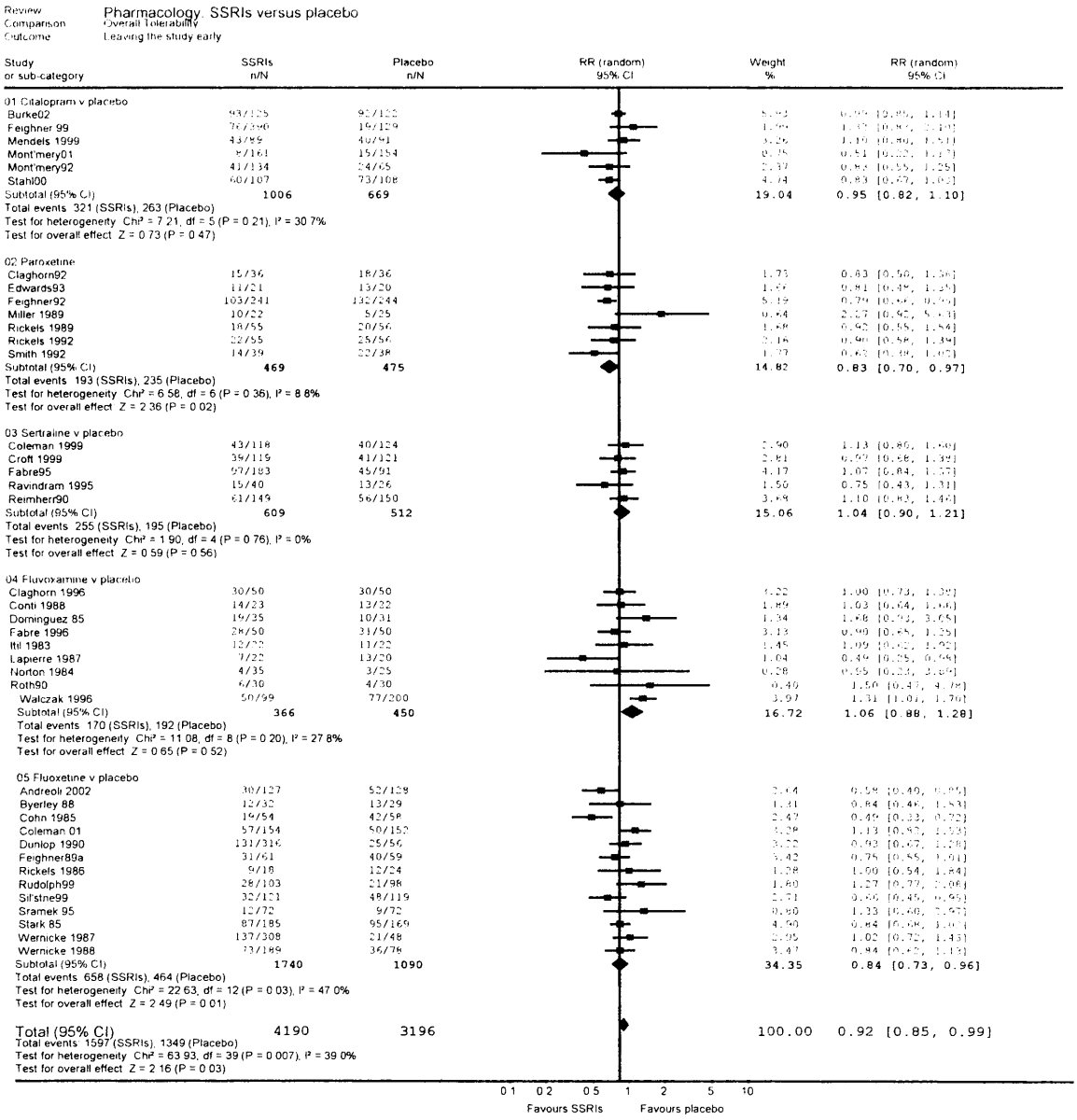
**Figure 3.5: SSRIs versus placebo: mean endpoint by severity**




## Comparison 2: Acceptability and tolerability of SSRIs compared with placebo

When leaving treatment early is taken as a proxy measure of the acceptability of the treatment (see Figure 3.6), there is evidence to suggest a statistically significant difference favouring placebo over SSRIs but it is doubtful whether it is of clinical significance (N= 39; n= 7274; RR= 0.92; 95% CI, 0.85 to 0.99). However, when the reasons for leaving the study early focus on side effects the difference is both statistically significant and likely to be clinically significant (N= 39; n= 7460; RR= 2.45; 95% CI, 2.08 to 2.89).

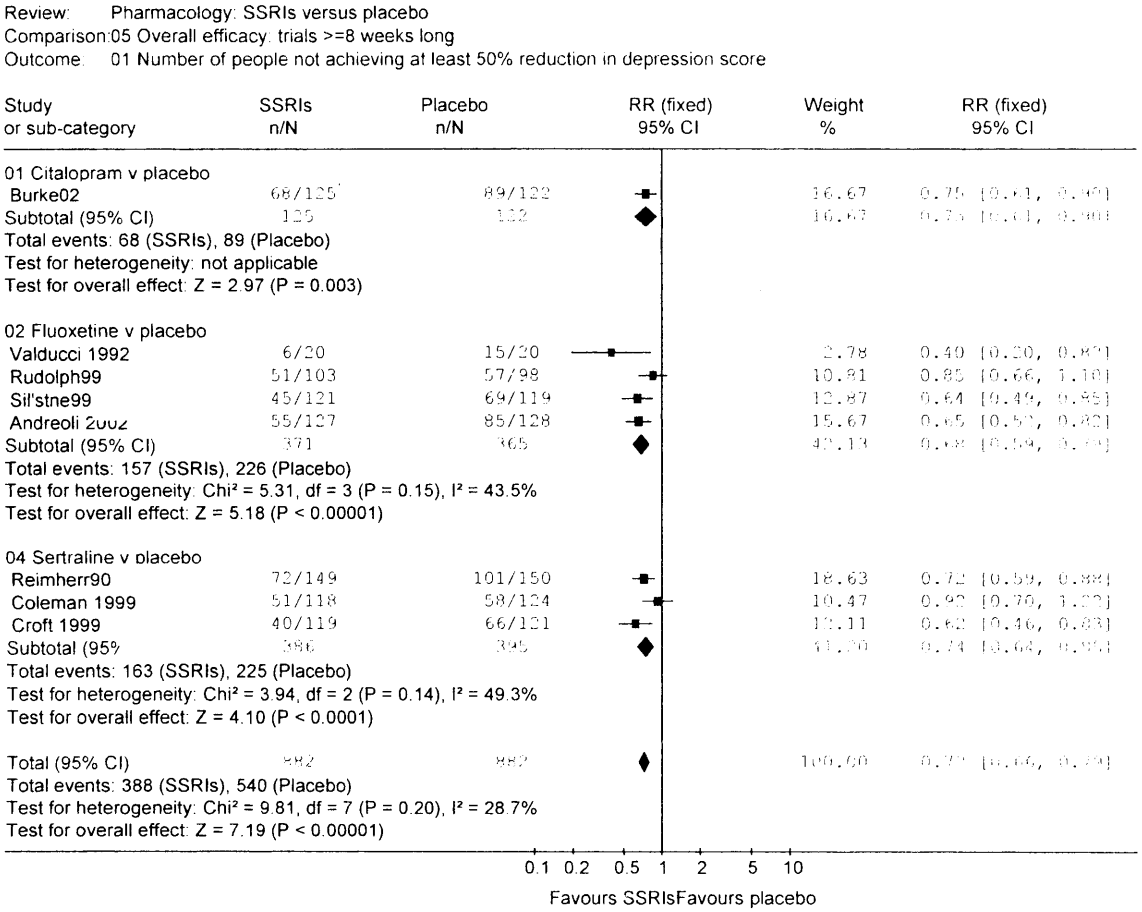
**Figure 3.6: SSRIs versus placebo: leaving the study early for any reason**




## Comparison 3: Sub-analysis of SSRIs versus placebo – effect of treatment on efficacy outcomes in trials lasting 8 weeks or longer

It has been argued that the placebo effect may be short-lived and therefore in order to assess this, a sub-analysis of trials lasting 8 weeks or longer was conducted. Examination of the data presented in Figure 3.7 suggests that the pattern of response in 8-week-plus trials mirrors that of shorter-duration trials. In trials lasting 8 weeks or longer, there was evidence, when considering a 50% reduction in depressive symptoms as measured by the HRSD, of a clinically significant benefit favouring SSRIs over placebo (N=8; n=1764; RR=0.72; 95% CI, 0.66 to 0.79).

**Figure 3.7: SSRIs versus placebo: trials over 8 weeks**




As was the case with SSRIs in the overall comparison with placebo, the evidence for achieving remission was weaker as measured by the HRSD (N=2; n=456; RR=0.85; 95% CI, 0.67 to 1.07). A similar picture emerges when continuous measures are considered, with no convincing evidence of a clinically important difference, although the difference is statistically significant (N= 7; n= 1369; SMD [random effects = -0.28; 95% CI, -0.44 to -0.11).

In moderate depression in trials lasting 8 weeks or longer, there is evidence suggesting that there is a statistically significant difference favouring SSRIs over placebo on reducing depression symptoms as measured by the HRSD, but the size of this difference is unlikely to be of clinical significance. For example, for moderate depression the RR was 0.75 (N= 3; n= 729; 95% CI, 0.65 to 0.87), for severe depression it was 0.63 (N= 3;

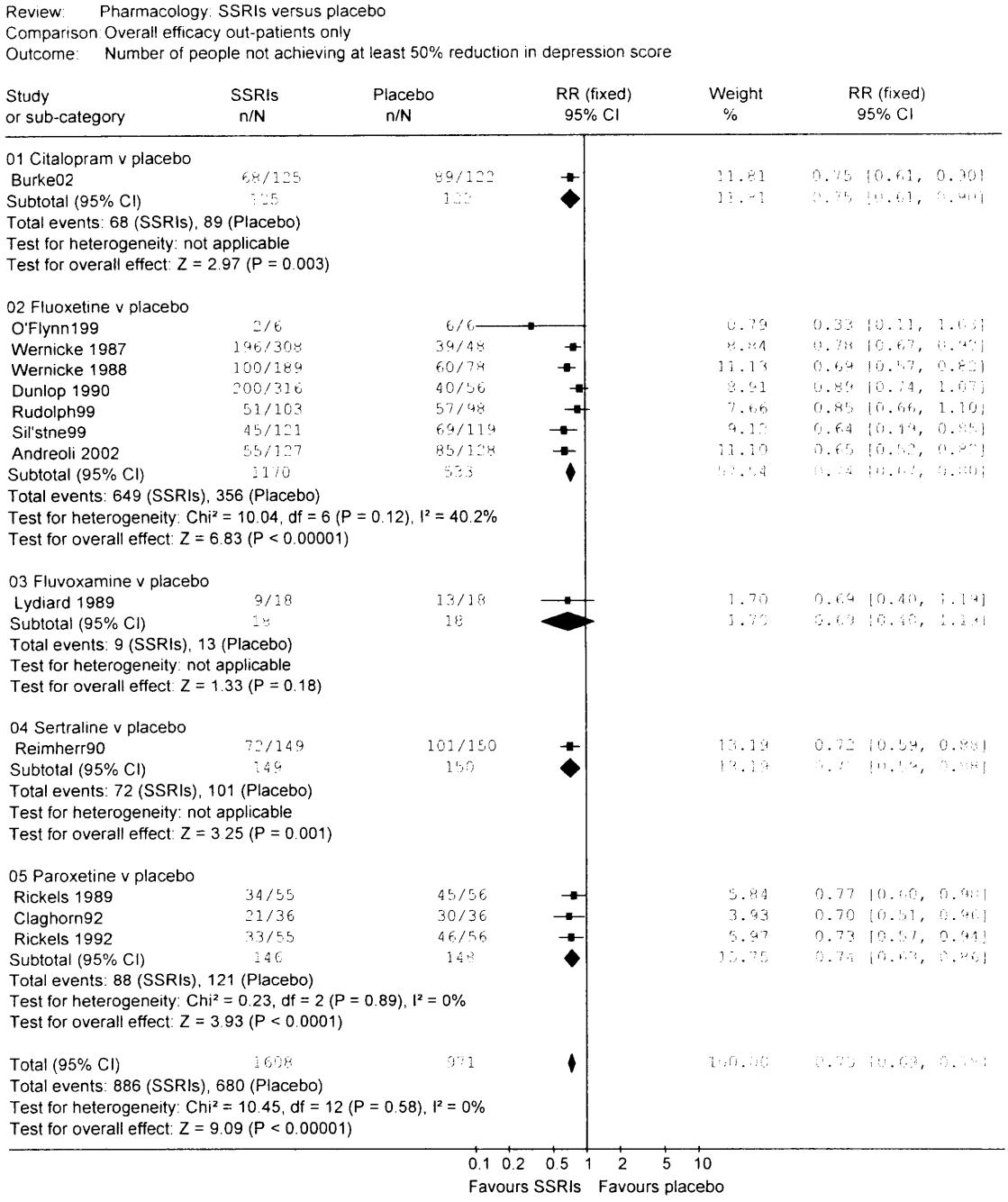
n= 535; 95% CI, 0.53 to 0.74) and in very severe depression it was 0.72 (N= 1; n= 299; 95% CI, 0.59 to 0.88). When outcomes on continuous measures (the HRSD) for different severities of depression are considered, again a similar pattern emerges with a statistical but probably not a clinically important difference for moderate depression (N= 2; n= 386; SMD= -0.28; 95% CI, -0.48 to -0.08), some limited evidence of a clinically significant difference for severe depression (N= 1; n= 237; SMD= -0.53; 95% CI, -0.79 to -0.27) and a statistically but possibly not clinically significant benefit for very severe depression (N= 1; n= 283; SMD= -0.43; 95% CI, -0.67 to -0.2). With regard to acceptability of SSRI treatment in trials lasting 8 weeks or longer, a very similar picture emerges with evidence suggesting that there is no clinically significant difference between SSRIs and placebo on reducing the likelihood of leaving treatment early (N= 13; n= 3069; RR [random effects] = 0.95; 95% CI, 0.83 to 1.09) but again for those who do leave treatment early, side effects appear to have a clinically significant effect (N= 13; n= 3069; RR [random effects] =1.93; 95% CI, 1.23 to 3.03).

**Comparison 4: Sub-analysis of SSRIs versus placebo – effect of treatment setting**

It was the intention to do a subgroup analysis on trials of SSRIs in primary care as it was expected that this population would most closely match those recruited into collaborative care studies. Unfortunately only one study (MONTGOMERY2001) took place in primary care and no data were extractable for response, remission or endpoint scores (data were only extractable for acceptability), so evidence directly relevant to collaborative care was not available. In view of this, the subset of the data relating to outpatients, as a possible proxy for primary care, was analysed separately; this excluded trial populations that included solely inpatient populations of mixed inpatient/outpatient populations.

As can be seen from Figure 3.8, the RR obtained for a 50% reduction in depressive symptoms for the outpatient subgroup is identical to that for the overall population (N = 13; n = 2579; RR = 0.73; 95% CI, 0.69 to 0.78).

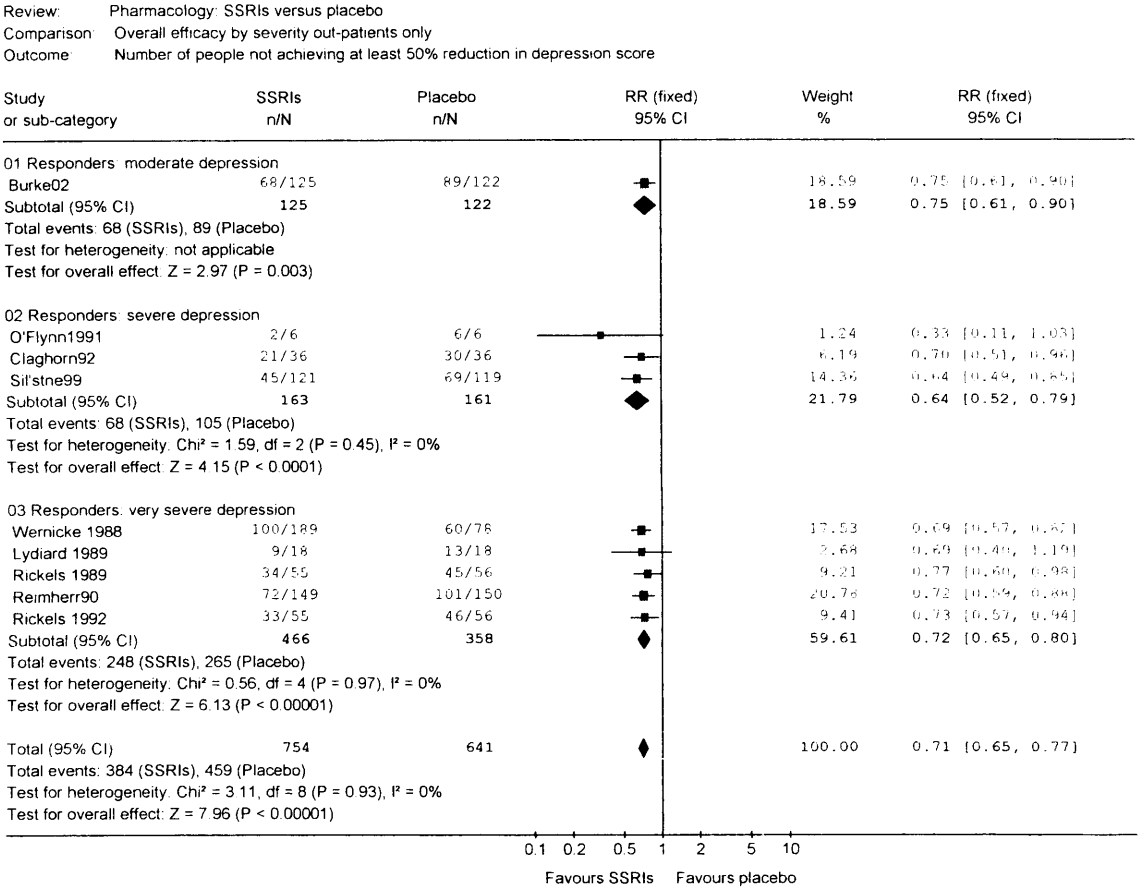
**Figure 3.8: SSRIs versus placebo: 50% reduction in depression score – outpatients only**




When severity of depression is considered, a very similar pattern emerges. As can be seen from Figure 3.9, while not identical, the RR for the outpatient-only population follows a very similar pattern. For moderate depression there is evidence of a clinically important difference favouring SSRIs on a 50% reduction in depressive symptoms, (N= 1; n= 247; RR= 0.75; 95% CI, 0.51 to 0.90). The picture is more positive for severe depression, with the analysis favouring SSRIs over placebo on a 50% reduction in

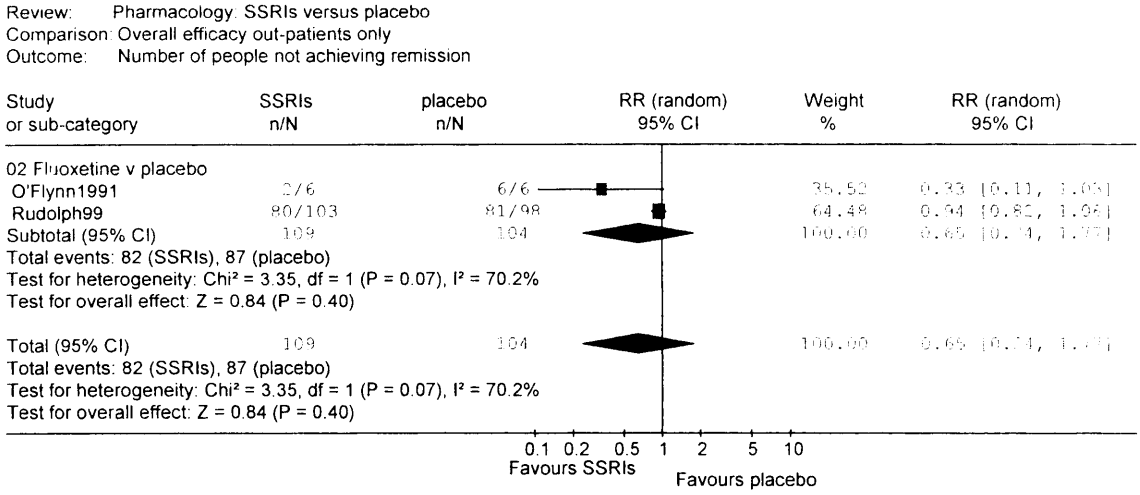
depressive symptoms (N= 3; n= 344; RR= 0.64; 95% CI, 0.52 to 0.79). However, the pattern of increasing benefit with severity is not seen for very severe depression, (N= 5; n= 824; RR= 0.72; 95% CI, 0.65 to 0.77).

**Figure 3.9: SSRIs versus placebo: 50% reduction in depression score by severity – outpatients only**




When remission for out-patients is considered (see Figure 3.10), the effect is larger but is not statistically significant, which might be expected with only two studies (N= 2; n= 213; RR [random effects] = 0.65; 95% CI, 0.24 to 1.77).

**Figure 3.10: SSRIs versus placebo: number not achieving remission – outpatients only**




## 3.6 Summary of the efficacy of SSRIs

The evidence reviewed above suggests that when a 50% reduction in depressive symptoms is used as the outcome there is good evidence for the efficacy of the SSRIs. The data also provide some evidence for the increased effectiveness of SSRIs over placebo in very severe depression. The effects identified in the longer-term trials (that is trials of 8 weeks and over) generally confirm the picture from the overall analysis of the data. However, as noted above, responder data is the least stringent test of the three outcomes used and, when remission is used as the outcome measure, the benefits of SSRIs over placebo is not so marked, with a trend to a smaller benefit being identified. The picture is even less convincing when continuous scores at endpoint are used, with a generally smaller effect size than was reported on either of the other two measures. Overall, SSRIs also produced more side effects than placebo, with more people leaving treatment early as a consequence. No useable data for primary care was identified and so an outpatient subgroup (in fact the majority of the trials) was analysed and a picture consistent with the overall efficacy picture for SSRIs emerged.

Examination of the standard deviations of scores reported in the trials suggests considerable variation in outcomes, which is reinforced by the high attrition rate in a number of the trials. This suggests that there may be considerable variation between individuals in their response to antidepressants, with some patients showing significant

benefit and others not. However, given the design of the trials it is not possible to identify any subgroups who may have responded particularly well to antidepressants.

### 3.7 Limitations of the review of SSRIs

This review of the SSRIs has several limitations. First, there was evidence from the forest plots of potential publication bias, which was confirmed by the MHRA report into the safety of SSRIs (MHRA, 2004). For example, although the report had available over 250 trials of fluoxetine, a further 250 trials were not made available to the review (MHRA, 2004) as these were completed before the rules governing good clinical practice for trials were implemented (European Medicines Agency, 2006). From the perspective of this thesis, the absence of a dataset on the efficacy of SSRIs in primary care settings is also a considerable limitation. It should be noted that many patients seen in primary care settings may have milder disorders and may therefore tend to remit more rapidly, and this may lead to an over-estimation of the effects of medication by clinicians in routine practice. Alternatively the overall higher remission rates may also mask the effect on a sub-group who may benefit from antidepressants. In addition, all trials were short term and provided no long-term outcome data. This largely reflects their primary purpose; that is, to establish the efficacy of SSRIs for licensing purposes. Also, the evidence for efficacy rests strongly on the weakest measure of those chosen; responder data and data from the other two outcomes overall produced less positive results. The focus on placebo studies and their primary role in licensing also means that populations that may present commonly in primary care, such as people with chronic or treatment-resistant depression, are also excluded from the review.

The above review and its limitations suggest some caution about the use of antidepressants as a treatment for depression but it should be remembered that, although the placebo effect may account for a significant proportion of the response (perhaps up to 80% [Kirsch *et al.*, 2002b]), comparison against waitlist may result in improvements of around 10 to 15 points on both the HRSD or the BDI-II (Kirsch *et al.*, 2002b). This, along with the difficulty in identifying who may respond to the placebo, suggests antidepressants still have an important role to play in the treatment of depression. If this is the case, ensuring that patients take antidepressants for sufficient duration is

important. Duration of antidepressant treatment and the issue of adherence to treatment are dealt with below.

### 3.8 The duration of antidepressant treatment

Depression is for many people a chronic disorder and one that therefore might warrant long-term or maintenance treatment. Geddes and colleagues (2002) report on a meta-analysis of continuation treatment with antidepressants, which provides important information in this area. They looked at the effects of continuing treatment with antidepressants in patients with depressive disorders who had responded to acute treatment. Their review included 31 RCTs involving nearly 4500 patients and reported a 70% reduction in relapse for those who continued with antidepressants following remission compared with those who were randomised to placebo. The average rate of relapse on placebo was 41% compared with 18% for those who continued taking an antidepressant and there was evidence that the treatment effect persisted for up to 36 months, although most of the trials were of shorter duration. This review therefore supports the observation that if a patient has benefited from antidepressant medication, staying on medication could confer a significant advantage. Unfortunately the majority of the people in the studies were patients from specialist mental health services with a high risk of relapse and this, along with the possibility that the withdrawal of the medication may have had a negative effect on some participants, requires that some caution be exercised in the application of these results to collaborative care interventions.

### 3.9 Adherence to antidepressant treatment

If the potential benefits of longer-term treatment are to be realised, two conditions need to hold. First, that the drugs are prescribed at an adequate dose and secondly that the regime of treatment is adhered to. There is reasonable evidence from a number of studies of prescribing databases that SSRIs, in contrast to TCAs, tend to be prescribed at the correct doses. For example, a UK prescribing study including data from over 750,000 patient records found that 99.9% of SSRIs were prescribed at the correct dose compared with only 13.1% of TCAs (Donoghue *et al.*, 1996). A further UK study of over 20,000 primary care patients found that at least 72% of those prescribed TCAs never received "an effective dose" compared with only 8% of those prescribed SSRIs

(MacDonald *et al.*, 1996). This would further support the use of SSRIs as first-line antidepressants in a collaborative care intervention.

A further advantage of SSRIs over TCAs can be seen in the adherence to long-term antidepressant regimes. Dunn and colleagues (1999), in a study of over 16,000 primary care patients prescribed either TCAs or SSRIs, reported that while 33% of those prescribed an SSRI were judged to have completed an adequate period of treatment (that is, prescriptions covering at least 120 days' treatment within the first 6 months after diagnosis) only 6% of those prescribed a TCA did. Of course this study does not account for the possibility that some patients may have switched medication and may have done so to their long-term benefit. However, evidence from studies of prescribing patterns in primary care suggests that if patients discontinue one form of antidepressant medication they often do not take another medication. For example, Isacsson and colleagues (1999), in a study of nearly 1000 patients, report that only 35% ever received one prescription and only a minority received further prescriptions but, of those who did, patients prescribed SSRIs were more likely to be still being prescribed them at 6 months (42%) than if they were prescribed a TCA (27%).

This presents a potentially worrying picture; the effects of antidepressants seem modest and adherence to treatment regimes is also limited. For example, Lingam and Scott (2002), in a systematic review report non-adherence rates between 10% and 60% for antidepressants, with an average around 40%. They were also able to identify only a few well-conducted studies designed to improve antidepressant adherence, with at best modest effects. Vergouwen and colleagues (2003) in a review of medication adherence specifically contrasted interventions such as educational interventions not associated with a collaborative care intervention with those adherence programmes nested in collaborative care interventions, such as those developed by Katon and colleagues (2002), and reported improved adherence and better clinical outcomes in the latter. This view of increased adherence to antidepressants in collaborative care was also supported by the meta-regression study of Bower and colleagues (2006), which suggests that collaborative care was associated with increased medication adherence.

### 3.10 Conclusion

The outcome of the meta-analysis conducted in this chapter would suggest that if remission of depressive symptoms is to be the target of the intervention then antidepressants alone are unlikely to achieve this for a significant proportion of people with depression. It reinforces the view that augmentation of antidepressant treatment with collaborative care and/or psychological interventions, at least for those with moderate and severe depression, should be considered. The evidence on the benefits of continued treatment for those at high risk of relapse and the possible increased adherence to medication in collaborative care programmes suggest that such programmes may enhance the benefits of antidepressants compared with those obtained in usual care.

# 4. The Efficacy of Psychological Interventions in the Treatment Depression and their Application to Collaborative Care

## 4.1 Psychological interventions for the treatment of depression

Formal psychological approaches to the treatment of depression have developed over the past 100 years (Freud, 1917; Roth & Fonagy, 2005) along with an expansion of psychological theories about the aetiology and maintenance of depression (Gilbert, 1992). More recently there have been significant developments in psychological therapies designed specifically for depression (for example, Beck *et al.*, 1979; Weissman *et al.*, 2000). There have been a number of systematic reviews of the psychological treatment of depression including their combined use with antidepressants (for example, Gloaguen *et al.*, 1998; Pampallona *et al.*, 2004; Roth & Fonagy, 2005), which have concluded that those treatments specifically designed for depression such as cognitive behavioural therapy (CBT; Beck *et al.*, 1979) and interpersonal psychotherapy (IPT; Weissman *et al.*, 2000) are probably more effective than non-specific treatments (such as psychodynamic psychotherapy) and are also as effective as antidepressant medication (DeRubeis *et al.*, 1999; Hollon *et al.*, 2002). There is also some evidence to support the use of attenuated forms of psychological treatment for depression such as guided self-help (Gellaty *et al.*, 2007). This emphasis on depression-focused psychological treatments is also seen in clinical guidelines for depression in the UK (NICE, 2004a), the US (Beutler *et al.*, 2000), and Australia (RANZCP, 2004), all of which recommend treatments such as CBT and IPT.

However, what the reviews have not addressed directly is the application of the evidence for the psychological treatment of depression to the delivery of collaborative care. In addition, the efficacy of psychological therapies for depression of different severities has not been as well evaluated which is also addressed in this chapter. The primary focus of this chapter is therefore the evaluation of formal psychological therapies for depression and their utility in collaborative care. A meta-analysis of the formal psychological interventions for depression is first presented and this is followed by a review of the effectiveness of guided self-help.

### 4.2 Collaborative care and psychological treatments

The analysis of enhanced care interventions by Cape and colleagues (2007) provides some understanding of the potential value of different psychological approaches to depression in collaborative care. In their review it is possible to identify for the *attached professional model* the effect of different psychological treatments for depression including CBT, IPT and counselling. However, for counselling the majority of the studies had populations with both anxiety and depressive disorders and therefore no separate analysis for counselling by diagnosis of depression was possible. For this mixed diagnostic group Cape and colleagues (2007) report an effect size for counselling of SMD -0.29 (N= 766; 95% CI -0.44, -0.14). The effect sizes for CBT for depression were SMD -0.27 (N= 653; 95% CI -0.44, -0.11) and for IPT SMD -0.44 (N= 185; 95% CI -0.73, -0.15). Given the effect sizes and overlapping confidence intervals this suggests modest and broadly comparable effects for all three interventions and is line with the results of similar meta-analyses of psychological interventions (Churchill *et al.*, 2001; Wampold *et al.*, 2002).[7] This is also consistent with other meta-analyses, for example Westen and Morrison (2001). The effect size for problem solving therapy was smaller with an SMD of -0.16 (N= 891; 05% CI -0.30, -0.02), although this included a number of studies of sub-syndromal or minor depression (for example, Williams *et al.* [2000]).

In a systematic review of psychological interventions in primary care that focused on their potential applicability to collaborative care, Brown and Schulberg (1995) concluded that problems associated with diagnostic classification, attrition rates and outcome measures limited the conclusions that could be drawn about effective psychological interventions. When considering specific studies of collaborative care, there are a number of additional reasons why it may be difficult to identify the particular contribution of psychological therapies to collaborative care. These include the use of psychological interventions in combination with antidepressant medication (Unutzer *et al.*, 2002; Simon *et al.*, 2004); the possibility of variable uptake of psychological therapies within the study protocols (such as the use of psychological therapies only by

[7] The outcomes for CBT for people with anxiety disorders in Cape and colleagues (2007) were substantially greater with an SMD of -1.28 (N= 128; 95% CI -1.71, -0.84).

those patients who refused or had not benefited from antidepressants, for example, Hedrick and colleagues [2003]); the use of psychological therapies by participants other than those directly provided in the study (Katon *et al.*, 1995; Smit *et al.*, 2006); and the differing purpose of psychological therapies used (for example, supporting medication adherence or directly treating depression) (Katon *et al.*, 1996; Simon *et al.*, 2004).

Of the 27 studies of collaborative care which Cape and colleagues (2007) reviewed, 10 provided some kind of psychological therapy. In two studies (Katon *et al.*, 1995; Katon *et al.*, 1999) the psychological therapy was not provided by clinicians directly involved in the trial but allowable within the study protocol. A further study (Katon *et al.*, 1996) provided brief cognitive therapy focused on supporting medication adherence as well as allowing for more broadly based psychological therapy outside that directly provided by the study and another problem solving as an alternative to medication (Katon *et al*, 2004). Of the remaining studies, two included a formal psychological therapy (CBT [Hunkeler *et al.*, 2002] or IPT [Bruce *et al.*, 2004]) as a part of a stepped care protocol where initial failure to benefit from or refusal to take an antidepressant resulted in referral for a psychological intervention. The other four studies involved the direct provision of individual or group CBT (Wells *et al.*, 2000; Smit *et al.*, 2006), the provision of CBT by telephone (Simon *et al.*, 2004), and problem solving therapy (Unutzer *et al.*, 2002). Uptake of the different psychological therapies varied considerably between these studies as did study design, the role of the "depression care managers", the role of primary care physicians and the diagnostic and inclusion criteria for the trials, which again made it difficult to identify what, if any, contribution the psychological interventions had made. (The effect size for the four studies involving direct provision of psychological was SMD -0.21 [N=1296; 95% CI -0.39, -0.12], again not very different from the effect size for collaborative care overall.)

However, it is informative to contrast the variability that exists in the provision of psychological therapy for collaborative care with the provision of medication. In most, if not all collaborative care studies, medication protocols are well described and their implementation is the focus of considerable effort in both early trials (for example, Katon *et al.*, 1995) and more recent studies (for example, Dietrich *et al.*, 2004; Simon *et al.*, 2004) where a significant proportion of the depression care specialists' time is devoted to medication adherence. Indeed, it has been suggested that the effect of

collaborative care is mediated in part through the effects of antidepressant medication (Bower *et al.*, 2006). This is not surprising because medication adherence is a consistent intervention in studies of collaborative care, but it leaves unanswered what the precise contribution of psychological therapies might be to the provision of effective collaborative care; however it should be noted that Bower and colleagues (2006) were not able to find an association between the provision of psychological therapies and improved outcomes.

### 4.3 Meta-analysis of psychological interventions for depression

#### Therapies considered for review

Two initial criteria were adopted when determining which psychological therapies to include in the review: the therapy should be available in the NHS (and therefore would potentially be available for use in a collaborative care intervention) and there should be evidence from existing reviews of a sufficient evidence base to warrant further investigation. Six formal psychological therapies are included in the review, which are listed below along with a brief description of the approach and a definition of the therapy that was used to identify whether or not the intervention in a particular study could be classified as one of the six formal psychological therapies. The reviews were limited to individual interventions as group interventions were not felt to be appropriate for use in an exploratory trial of a collaborative care intervention.

#### Cognitive behavioural therapy (CBT)

CBT for depression was developed by Beck during the 1950s and 1960s and was formalised into a treatment in the late 1970s (Beck *et al.*, 1979). The treatment focuses on cognition and adopts a collaborative, educative approach in which the depressed person learns to recognise his or her negative thinking patterns and how to re-evaluate them. Individuals are encouraged to practise re-evaluating their thoughts and engage in new behaviours during and outside of treatment sessions. The approach eschews unconscious conflicts, transference or interpretation of psychodynamic therapy.

*Definition* - CBT was defined as a discrete, time-limited, structured psychological intervention, derived from the cognitive model of depression where the patient:

- Works collaboratively with the therapist to identify the types and effects of thoughts, beliefs and interpretations on current symptoms, feelings states and/or problem areas.
- Develops skills to identify, monitor and then counteract negative thoughts, beliefs and interpretations related to the target symptoms/ problems.
- Learns a repertoire of coping skills appropriate to the target thoughts, beliefs and/or problem areas.

**Behaviour therapy (BT)**

BT, (also often referred to as "behavioural activation") for depression, developed from learning theory (for example, Lewinsohn, 1975; Martell *et al.*, 2004). In this approach depression is seen as the result of a low rate of positively rewarded behaviour and the focus is on behavioural activation aimed at encouraging the patient to develop more rewarding behaviours (Lewinsohn, 1975). Recently there has been renewed interest in behavioural activation with a focus not only on engaging in pleasant activities, but also on the problems of avoidance and the development of skills to tolerate and accept difficult feelings and situations (Martell *et al.*, 2004).

*Definition* - BT was defined as a discrete, time-limited, structured psychological intervention, derived from the behavioural model of depression and where the therapist and patient:

- Work collaboratively to identify the effects of behaviours on current symptoms, feelings states and/or problem areas.
- Seek to reduce symptoms and problematic behaviours through behavioural tasks related to: reducing avoidance, graded exposure, activity scheduling, behavioural activation and increasing positive behaviours.

**Interpersonal psychotherapy**

IPT was developed by Klerman and Weissman (Klerman *et al.*, 1984) and focuses on current relationships and interpersonal processes rather than intrapsychic ones. It is time limited and seeks to help patients link their mood with their behaviour and to recognise that, by addressing interpersonal problems, they may improve both their relationships and their mood. The intervention is structured around four key conflict areas: role transitions, interpersonal role disputes, grief and interpersonal deficits (Weissman *et al.*, 2000). Treatment focuses on facilitating the understanding of interpersonal interactions and exploring alternative ways of handling difficult interpersonal situations.

*Definition* - IPT was defined as a discrete, time-limited, structured psychological intervention, derived from the interpersonal model of depression that focuses on interpersonal issues and where therapist and patient:

- Work collaboratively to identify the effects of key problematic areas related to interpersonal conflicts, role transitions, grief and interpersonal skills, and their effects on current symptoms, feelings states and problems.
- Seek to reduce symptoms by learning to cope with or resolve these interpersonal problem areas.

**Problem solving therapy**

Difficulties in dealing with problems have long been recognised as a central problem in depression (Nezu, 1989). Several types of problem solving therapy for depression have been developed and include 'social problem solving therapy' developed by Nezu (1989), which is group based and focuses both on developing problem solving skills and the attitudes that may inhibit attempts to engage in problem solving tasks. Another individually-based version of problem solving therapy was developed by Mynors-Wallis and colleagues (1995) and concentrates on developing goal-focused, problem solving skills. It was developed in the UK specifically for primary care and it is this form of problem solving that is the focus of this review.

*Definition* – Problem solving therapy was defined as a discrete, time-limited, structured psychological intervention, which focuses on learning to cope with specific problems areas and where:

- Therapist and patient work collaboratively to identify and prioritise key problem areas, to break problems down into specific, manageable tasks, problem solve, and develop appropriate coping behaviours for problems.

**Counselling**

Counselling was developed by Rogers (1957) who believed that people had the means for self-healing, problem resolution and growth if the right conditions could be created. These conditions include the provision of positive regard, genuineness and empathy. Rogers's original model was developed into a structured counselling approach by Truax and Carkhuff (1967) although many other therapies now use the basic elements of client-centred counselling (Roth & Fonagy, 2005). Today, however, counselling is more often used as a generic term used to describe a broad range of interventions delivered by "counsellors" usually working in primary care; the various approaches may include psychodynamic, systemic or cognitive behavioural interventions (Bower *et al.*, 2003).

*Definition* - For this review counselling was defined as a discrete, usually time-limited, psychological intervention, broadly in line with Rogers' original conceptualisation, where:

- The intervention has a facilitative approach often with a strong focus on the therapeutic relationship and the development of positive regard, genuineness and empathy, but which may also be structured and, at times, directive.

**Short-term psychodynamic psychotherapy**

Psychodynamic psychotherapy is a derivative of psychoanalysis (Freud, 1917) and there are now a number of variations of the original model (Malan, 1995; Holmes, 2001; Luborsky, 2003), but all retain a central emphasis on the importance of unconscious processes and the therapeutic relationship (including transference and counter-transference). Typically short-term, psychodynamic therapy is provided over a period of 10-20 weeks involving up to 40 hours of treatment (Leichensring *et al.*, 2004; Abbas *et al.*, 2006).

*Definition* - Short-term psychodynamic interventions were defined as psychological interventions, derived from a psychodynamic/psychoanalytic model, and where:

- Therapist and patient explore and gain insight into conflicts and how these are represented in current situations and relationships including the therapeutic relationship (for example, transference and counter-transference).
- This leads to patients being given an opportunity to explore feelings, and conscious and unconscious conflicts, originating in the past, with a technical focus on interpreting and working though conflicts.
- Therapy is non-directive and recipients are not taught specific skills (for example, thought monitoring, re-evaluating, or problem solving).

### 4.4 Method

The method adopted for this review followed that of the systematic review of pharmacological interventions in Chapter 3. Filters were developed for specific psychological interventions and are set out in Appendix H. The initial searches were undertaken in January 2003, with update searches being carried in August 2006.

#### Outcomes

The main outcome measures were the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) and the Beck Depression Inventory (Beck *et al.*, 1961; 1996) endpoint scores (any version), since these are the most widely reported measures in the included studies and are accepted as reasonable measures of depression symptoms (American Psychiatric Association, 2000). Remission was extracted as a secondary measure (reported as non-remission for statistical reasons) as this outcome was often not reported in psychological treatment trials. Study attrition rates (any reason and specifically due to side effects) were additional secondary measures.

#### Identification of studies

The initial search identified 5,235 reports, and updates revealed a further 57 papers. In addition, reference lists of identified studies were hand-searched, and known researchers in the field contacted for details of unpublished studies. Details of all papers relevant to the review are included in Appendix I.

All data were entered into entered into Review Manager 4.2 (Cochrane Collaboration, 2003). Forest plots of the main outcomes, in particular where they are multiple studies in the forest plot, are included in the body of the text.

### 4.5 Cognitive behavioural therapy (CBT)

A total of 32 trials were identified for CBT, which included 19 from the US, 10 from the UK and 3 from Europe. In all, data from 3,421 participants were identified. A total of 65 trials were excluded; details on included trials can be found in Appendix J.

There were 20 studies of individual CBT for patients with a primary diagnosis of depression at baseline, six of which included follow-up data (BLACKBURN1981, BLACKBURN1997, GALLAGHER-THOMPSON1994, HAUTZINGER1994, MURPHY1984, SHAPIRO1996). A further study included a range of diagnoses at baseline with 62% having a primary diagnosis of depression (WARD2000).[8] Two additional studies looked at CBT for patients with residual symptoms after initial treatment (FAVA1994 and PAYKEL1999) and both included follow-up measures. A further two studies looked at continuation treatment in treatment responders (JARRETT2001, TEASDALE2000), while two others included both an acute phase plus a continuation phase in treatment responders (DERUBEIS2005, DIMIDJIAN2006). Four studies compared group CBT with other group therapies (BEUTLER1991, BRIGHT1999, COVI1987, KLEIN1984), one of which included follow-up (BEUTLER1991).

There was considerable variation between studies on a number of variables including: the baseline severity of depression; therapist experience and training (where specified); setting and source of patients, including inpatient, outpatient, primary care and volunteer studies; treatment duration from 6 to 21 weeks and number of sessions provided from 6 to 25.

#### Comparison 1: CBT compared with antidepressants

Antidepressants are accepted as the standard treatment for depression therefore this is an important comparison. In addition to the provision of antidepressant drugs some trials in

[8] Since this was a large primary care based study comparing CBT with counselling and GP care, it is included in the review of counselling and short-term psychological therapies where there is little other RCT-level evidence.

this comparison provided "clinical management" (see Chapter 2) (ELKIN1989, DERUBEIS2005, DIMIDJIAN2006, HAUTZINGER1996 (data from two groups of patients in this study are reported separately), JARRETT1999, KELLER2000, THOMPSON2001). In MIRANDA2003 participants received weekly telephone calls to assess adverse effects, adherence and treatment effects. In the remaining trials, either this is not mentioned (BLACKBURN1981, SCOTT1992) or participants received non-manualised general support (BLACKBURN1997, MURPHY1984). The data for this comparison is summarised in Figure 4.1.

**Figure 4.1: CBT versus antidepressants**

Review: Psychology: CBT
Comparison: CBT v ADs (with/without Clinical Management or GP care)
Outcome: Depression scores: continuous measures post-treatment

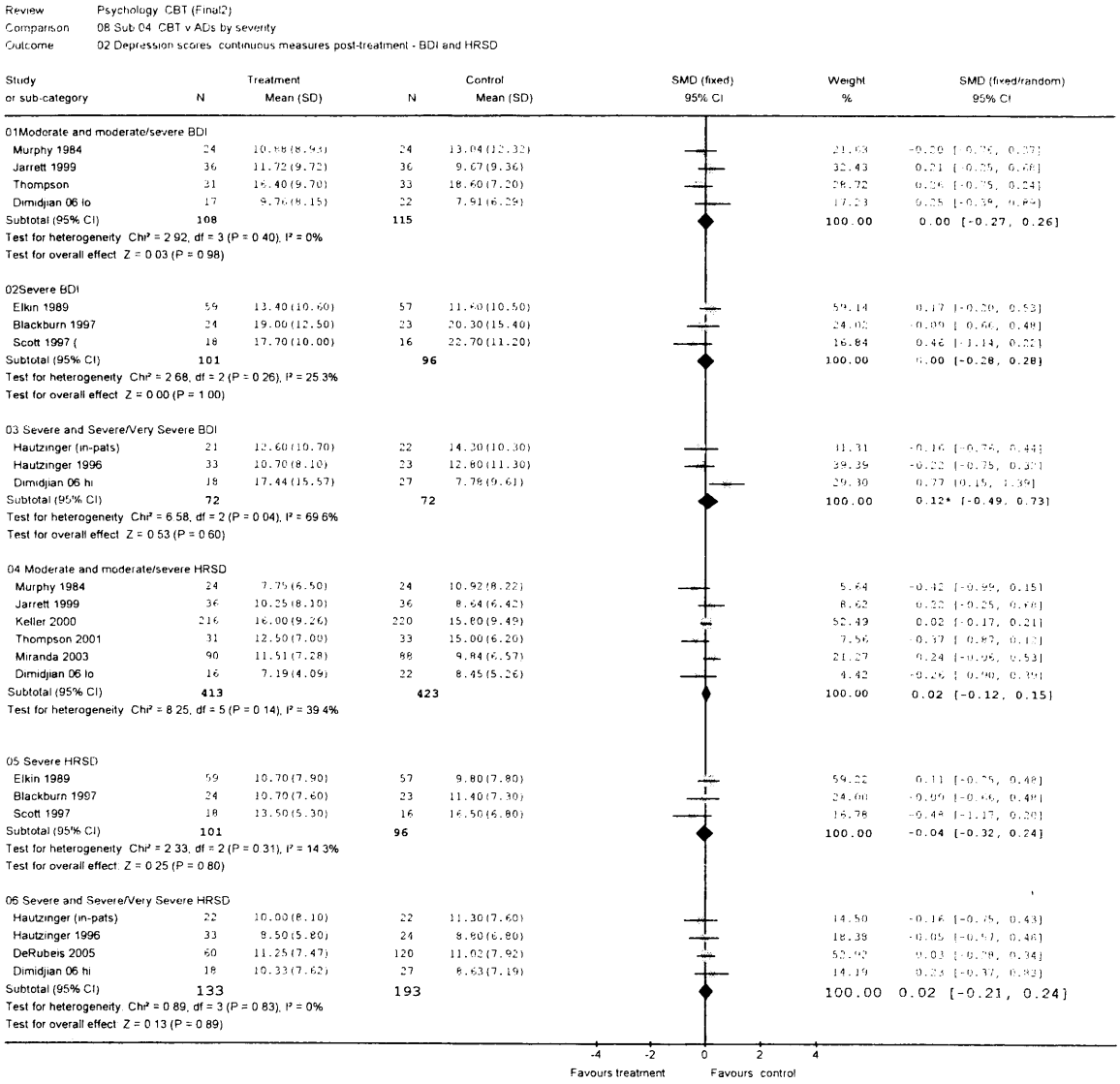
| Study or sub-category | N | Treatment Mean (SD) | N | Control Mean (SD) | SMD (random) 95% CI | Weight % | SMD (random) 95% CI |
|---|---|---|---|---|---|---|---|
| 01 BDI scores post-treatment | | | | | | | |
| Blackburn 1997 | 24 | 19.00(12.50) | 23 | 20.30(15.40) | | 8.65 | -0.09 [-0.66, 0.48] |
| Dimidjian 06 hi | 18 | 17.44(15.57) | 27 | 7.78(9.61) | | 7.44 | 0.77 [0.15, 1.39] |
| Dimidjian 06 lo | 17 | 9.76(8.15) | 22 | 7.91(6.29) | | 7.08 | 0.25 [-0.38, 0.89] |
| Elkin 1989 | 59 | 13.40(10.60) | 57 | 11.60(10.50) | | 19.79 | 0.17 [-0.20, 0.53] |
| Hautzinger (in-pats) | 21 | 12.60(10.70) | 22 | 14.30(10.30) | | 7.93 | -0.16 [-0.76, 0.44] |
| Hautzinger 1996 | 33 | 10.70(8.10) | 23 | 12.80(11.30) | | 9.85 | -0.22 [-0.75, 0.32] |
| Jarrett 1999 | 36 | 11.72(9.72) | 36 | 9.67(9.36) | | 12.84 | 0.21 [-0.25, 0.68] |
| Murphy 1984 | 24 | 10.88(8.93) | 24 | 13.04(12.32) | | 8.79 | -0.20 [-0.76, 0.37] |
| Scott 1997 | 18 | 17.70(10.00) | 16 | 22.70(11.20) | | 6.16 | -0.46 [-1.14, 0.22] |
| Thompson 2001 | 31 | 16.40(9.70) | 33 | 18.60(7.20) | | 11.47 | -0.26 [-0.75, 0.24] |
| Subtotal (95% CI) | 281 | | 283 | | | 100.00 | 0.01 [-0.19, 0.21] |
| Test for heterogeneity: Chi² = 12.39, df = 9 (P = 0.19), I² = 27.4% | | | | | | | |
| Test for overall effect: Z = 0.13 (P = 0.90) | | | | | | | |
| 02 HRSD scores post-treatment | | | | | | | |
| Blackburn 1997 | 24 | 10.70(7.60) | 23 | 11.40(7.30) | | 4.09 | -0.09 [-0.66, 0.48] |
| DeRubeis 2005 | 60 | 11.25(7.47) | 120 | 11.02(7.92) | | 12.40 | 0.03 [-0.28, 0.34] |
| Dimidjian 06 hi | 18 | 10.33(7.62) | 27 | 8.63(7.19) | | 3.76 | 0.23 [-0.37, 0.83] |
| Dimidjian 06 lo | 16 | 7.19(4.09) | 22 | 8.45(5.26) | | 3.24 | -0.26 [-0.90, 0.39] |
| Elkin 1989 | 59 | 10.70(7.90) | 57 | 9.80(7.80) | | 9.38 | 0.11 [-0.25, 0.48] |
| Hautzinger (in-pats) | 22 | 10.00(8.10) | 22 | 11.30(7.60) | | 3.84 | -0.16 [-0.75, 0.43] |
| Hautzinger 1996 | 33 | 8.50(5.80) | 24 | 8.80(6.80) | | 4.80 | -0.05 [-0.57, 0.48] |
| Jarrett 1999 | 36 | 10.25(8.10) | 36 | 8.64(6.42) | | 6.07 | 0.22 [-0.25, 0.68] |
| Keller 2000 | 216 | 16.00(9.26) | 220 | 15.80(9.49) | | 26.58 | 0.02 [-0.17, 0.21] |
| Miranda 2003 | 90 | 11.51(7.28) | 88 | 9.84(6.57) | | 13.47 | 0.24 [-0.06, 0.55] |
| Murphy 1984 | 24 | 7.75(6.50) | 24 | 10.92(8.22) | | 4.09 | -0.42 [-0.99, 0.15] |
| Scott 1997 | 18 | 13.50(5.30) | 16 | 16.50(6.80) | | 2.90 | -0.48 [-1.17, 0.20] |
| Thompson 2001 | 31 | 12.50(7.00) | 33 | 15.00(6.20) | | 5.38 | -0.37 [-0.87, 0.13] |
| Subtotal (95% CI) | 647 | | 712 | | | 100.00 | 0.01 [-0.10, 0.12] |
| Test for heterogeneity: Chi² = 11.59, df = 12 (P = 0.48), I² = 0% | | | | | | | |
| Test for overall effect: Z = 0.17 (P = 0.87) | | | | | | | |

-10 5 0 5 10
Favours treatment Favours control

As can be seen the results suggest no clinically significant differences between CBT and antidepressants on reducing depressive symptoms by the end of treatment (BDI: N = 8, n = 564; SMD [random effects] = 0.01; 95% CI, -0.19 to 0.21; HRSD: N = 11, n = 1359; SMD = 0.01; 95% CI, -0.10 to 0.12). In addition, no difference emerged when

data on remission was considered (HRSD: N = 6, n = 601; RR [random effects] = 0.98; 95% CI, 0.86 to 1.12).

**Figure 4.2: CBT versus antidepressants by severity (* indicates random effects)**




Interestingly, a sub-analysis by severity (see Figure 4.2) also failed to show any significant differences between antidepressants and CBT based on severity of depression as measured at baseline for moderate or moderate to severe depression (HRSD: N = 6, n = 836; SMD[random effects] = -0.02; 95% CI, -0.22 to 0.19; BDI: N = 4, n = 223; SMD = 0; 95% CI, -0.27 to 0.26); for severe depression (HRSD: N= 3, n= 197; SMD = -0.04; 95% CI, -0.32 to 0.24; BDI: N= 3, n= 197; SMD= 0; 95% CI, -0.28 to 0.28); or for severe to very severe depression (HRSD: N= 3, n= 326; SMD= 0.02; 95% CI, -0.21 to 0.24; BDI: N= 3, n= 144; SMD= -0.12; 95% CI, -0.48 to 0.73).

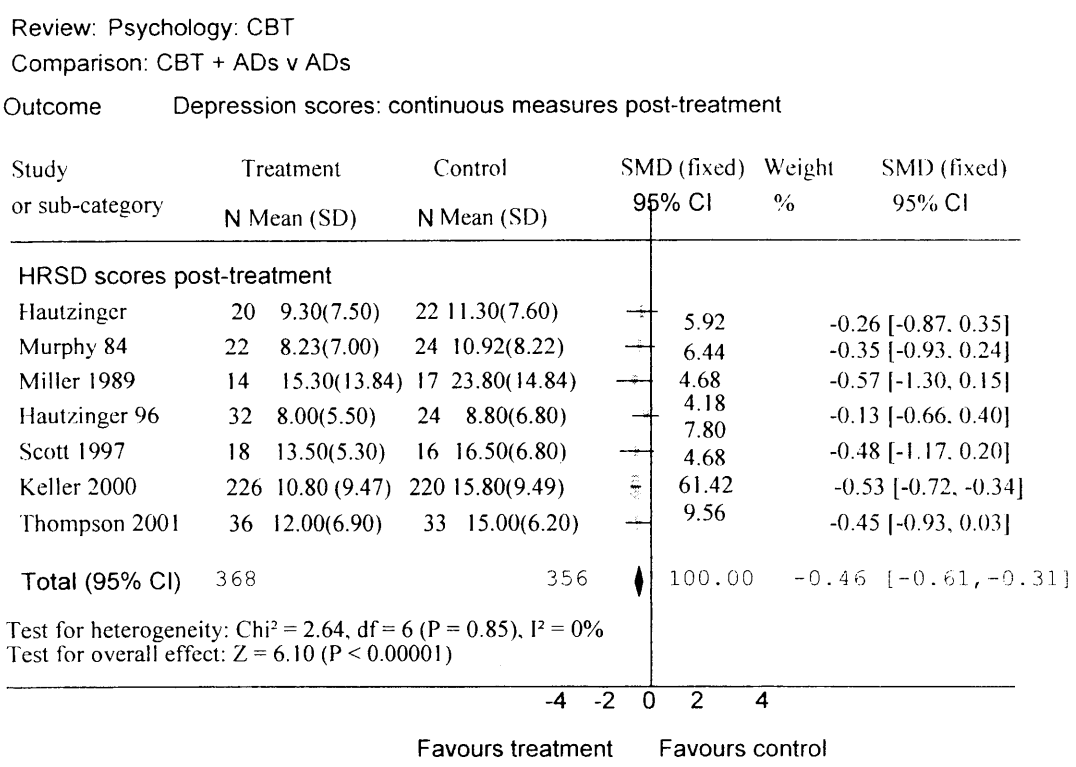
However, a different picture emerges 1 year after treatment, where CBT may be associated with maintaining a reduction of symptoms compared with antidepressants (HRSD: N=3; n= 137; SMD = -0.5; 95% CI, -0.84 to -0.15) and a reduction in the risk of relapse (N=4; n= 155; RR = -0.54; 95% CI, -0.37 to -0.78). This position is maintained at 2 years, albeit with a smaller data set on continuous measures (HRSD: N=1; n= 43; SMD = -0.37; 95% CI, -0.98 to -0.23) and a reduction in the risk of relapse (N=3; n= 107; RR = -0.6; 95% CI, -0.45 to -0.79). When the acceptability of the intervention is measured by drop-out from treatment there is some evidence suggesting that there is a significant difference favouring CBT over antidepressants (N= 11; n= 1187; RR= 0.74; 95% CI, 0.61 to 0.90).

**Comparison 2: CBT combined with antidepressants compared with antidepressants alone**

The majority of patients receiving psychological interventions in the NHS may also have been prescribed an antidepressant even if their compliance with the medication is poor. This may be because the clinician feels they would benefit from combined treatments or because they have been waiting for psychological treatment. The comparisons of psychological and pharmacological treatments against combined treatment are therefore of considerable importance. The data in Figure 4.3 shows that the addition of CBT to antidepressant treatment significantly improves outcomes on symptoms at the end of treatment (HRSD: N= 9, n= 724; SMD = -0.46; 95% CI -0.61, -0.31).

The data also suggests that the effect of combined treatment is greater with severe depression (HRSD for moderate depression: N= 2, n = 115; SMD = -0.41; 95% CI -0.78, -0.04; HRSD for severe depression: N= 3, n = 511; SMD = -0.53; 95% CI -0.7, -0.35). For relapse combined treatment is again more effective compared with taking antidepressants alone (HRSD: N= 3, n= 530; RR = 0.7; 95% CI 0.61, 0.80). Although it was not possible to detect a statistically significant difference between CBT plus antidepressants and antidepressants alone on reducing the likelihood of patients leaving treatment early for any reason, there was a trend favouring combination treatment (N = 8; n = 831; RR = 0.81; 95% CI, 0.65 to 1.01).

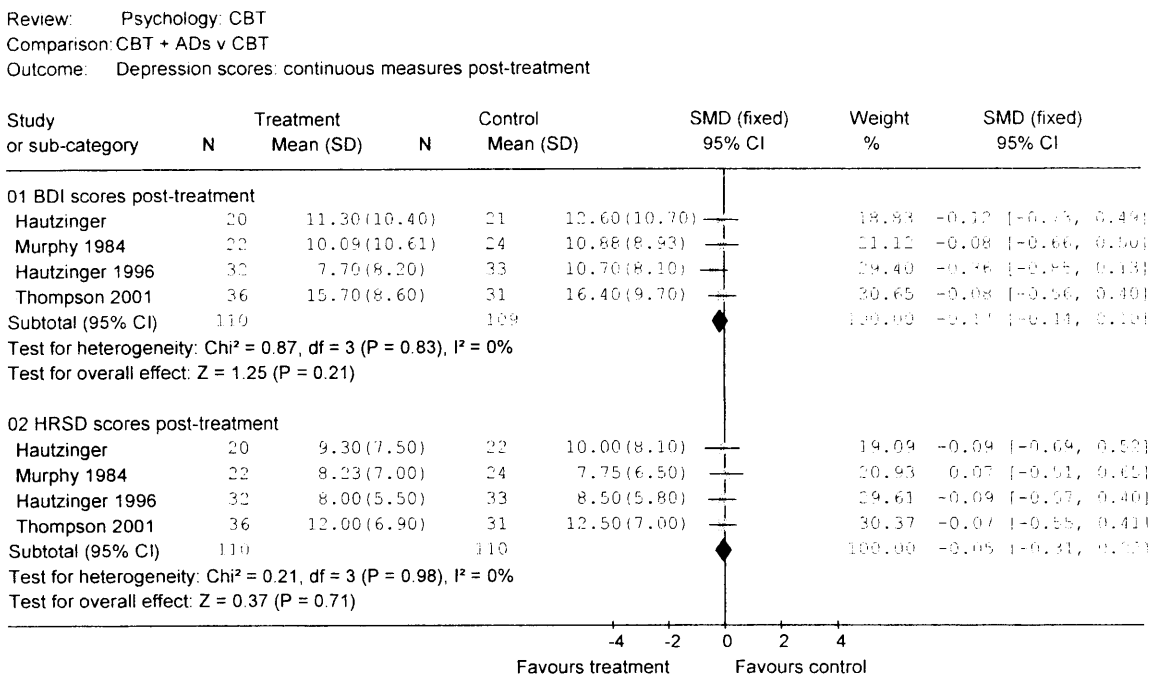
**Figure 4.3: Combined treatment versus antidepressants alone**




## Comparison 3: CBT combined with antidepressants compared with CBT alone

The evidence from the comparison above suggests that the addition of CBT to antidepressants increases the benefits obtained over antidepressants alone. The question then arises as to whether or not the addition of antidepressants to CBT confers an advantage over CBT alone. This comparison is more limited as there were only five trials available, in contrast to the addition of antidepressants to CBT does not seem to confer any advantage over CBT alone (Figure 4.4). (HRSD: N = 4; n = 220; SMD = -0.05; 95% CI, -0.31to 0.22). No differences emerge on the acceptability of treatment (N = 5; n = 710; RR = 1; 95% CI, 0.77 to 1.30).

**Figure 4.4: Combined treatment versus CBT**




## Comparison 4: Individual CBT compared with usual GP care

Of particular interest from the perspective of collaborative care is the comparison between CBT and treatment usually offered in primary care. Three studies compared individual CBT in primary care with usual GP care (SCOTT1992, SCOTT1997, FREEMAN[9]). There was insufficient evidence to determine whether there is a clinically significant difference between CBT provided in primary care and GP care (with antidepressant treatment) on reducing depressive symptoms at the end of treatment (BDI: n=2, N=92; SMD -0.33 [-0.74, 0.08]; HRSD: n=2, N=110; SMD -0.15 95% CI [-0,22, 0.52]). It is interesting to note that despite the use of more stringent criteria for the selection of studies in this review than were adopted by Cape and colleagues (2007) similar effect sizes were obtained (SMD -0.27 n=7, N=653 -0.27 95% CI [-0.44, -0.11]).

## Comparison 5: Individual CBT compared with other individual psychological interventions

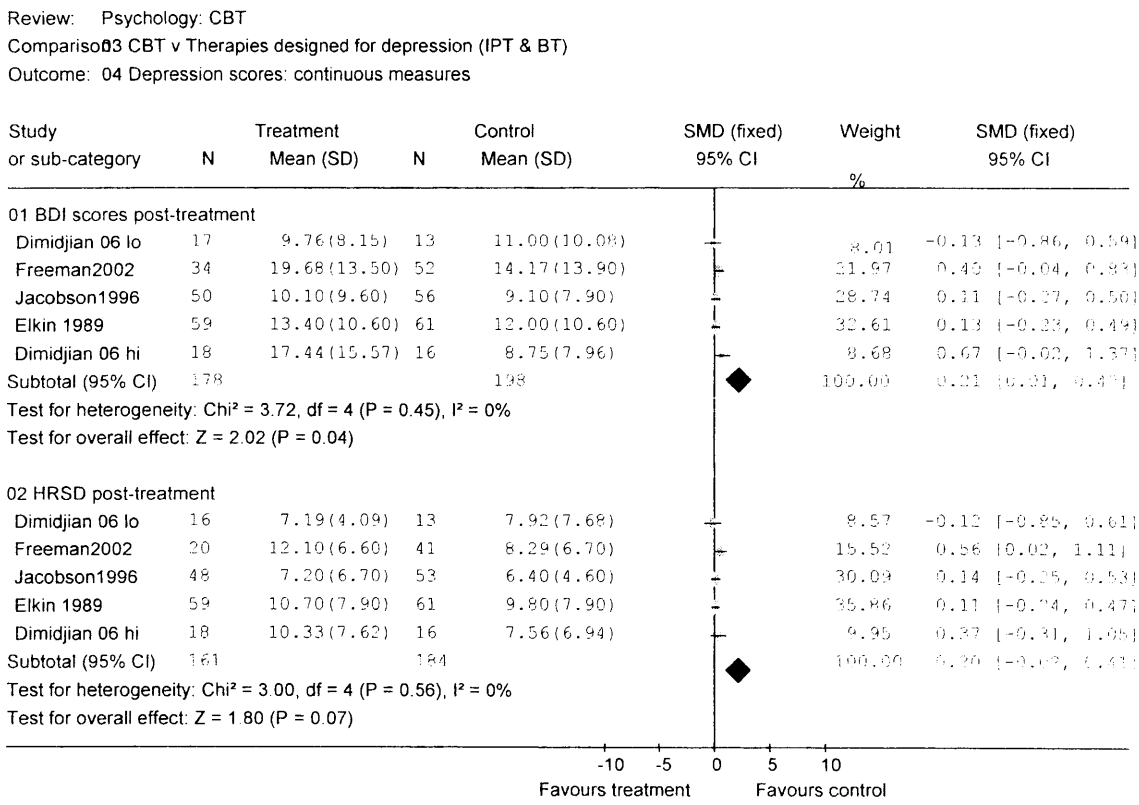
While the largest data set for a psychological therapy is for CBT, other psychological treatments have been evaluated and the main comparisons are described under separate headings below. In this section CBT is compared first with individual therapies

[9] The HRSD data were not extracted from FREEMAN because more than 50% of the participants in the CBT group were missing from this outcome.

specifically designed for the treatment of depression (that is, IPT and BT). In the first comparison, there are five trials: ELKIN1989 (IPT), DIMIJIDAN2006 (BT), FREEMAN2002 (IPT), GALLAGHER1982 (drop out data only) and JACOBSON1996 (BT). Then CBT is compared with other non-depression-specific therapies from three trials: GALLAHGER1973 (short-term psychological treatments-STPT), SHAPIRO1994 (STPT) and ROSNER1999 (Gestalt therapy).

In the first comparison (Figure 4.5) there is a small but statistically significant difference favouring other depression-specific treatments when compared with CBT at the end of treatment (BDI: N= 4, n = 376; SMD = 0.21; 95% CI, 0.01 to 0.42; HRSD:

**Figure 4.5: CBT versus non-CBT depression-specific interventions**




N= 4, n = 345; SMD = 0.20; 95% CI, -0.02 to 0.41). This difference is no longer statistically significant at 6-month follow-up (BDI: N= 2, n = 167; SMD = 0.18; 95% CI - 0.13 to 0.49; HRSD: N= 2, n = 155; SMD = 0.09; 95% CI, -0.23 to 0.40). On remission at end of treatment the difference is not clinically or statistically significant (BDI > 9: N= 2, n = 159; RR=1.26; 95% CI, 0.89 to 1.78). Similarly no difference in the

acceptability of the treatment as measured by leaving the study early was observed (N = 5, n = 443; RR=1.01; 95% CI, 0.58 to 1.77). This comparison suggests there is at least equivalence for depression-specific treatments with some suggestion of a possible advantage for non-CBT depression-specific treatments.

In the second comparison (non-depression specific treatments) there is a smaller data set limited to three small studies, and again no clinically or statistically significant results emerge. Here, the trend is in the opposite direction to that identified with depression-specific treatment comparisons. For example, at the end of treatment (BDI: N = 3, n = 59; SMD [random effects] = -0.19; 95% CI, -0.86 to 0.49; RDC criteria: N = 1, n = 66; RR = 0.59; 95% CI, 0.34 to 1.03) the difference favours CBT but it is neither clinically nor statistically significant.

**Summary of the effectiveness of CBT**

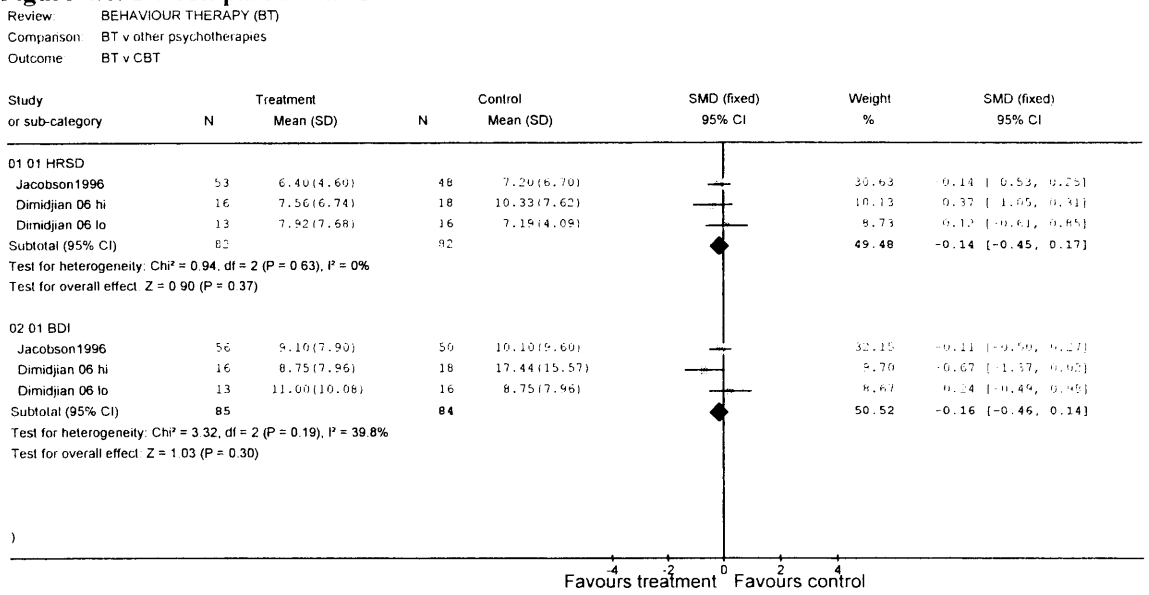
This review confirms that CBT is as effective as antidepressants in reducing depressive symptoms by the end of treatment, although it should be remembered that the effects of antidepressants are modest when compared with placebo. More importantly, there is some evidence to suggest that the effects of CBT are maintained a year after treatment whereas this may not be the case in those treated with antidepressants, unless the patient has responded and is maintained on antidepressants (Geddes *et al.*, 2002). The addition of CBT to antidepressants is more effective than treatment with antidepressants alone and is probably also cost effective (Simon *et al.*, 2006). The evidence for the addition of antidepressants to CBT is less convincing but the conclusions are limited by the relatively small data set. Comparisons of CBT against other active treatments provide no evidence of a clear benefit for any particular type of intervention but suggest that other depression-specific treatments (that is, IPT and BT) may be at least as effective as CBT at the end of treatment, whereas for other treatments (including STPT) there is some suggestion that CBT may be more effective.

### 4.6 Behaviour therapy

From the initial search four RCTs satisfied the inclusion criteria (GALLAGHER1983, HOPKO2003, JACOBSON1996 and MCLEAN1979), with six being excluded. A fifth trial (DIMAIDJIAN2006) was found from consultation with the advisors. The five studies contained a total of 310 patients and ranged from small brief treatments for

inpatients (HOPKO2003) to larger scale studies of outpatients of different severities. One (JACOBSON1996) was designed primarily to ascertain the effective components of CBT. Data were not extracted from MCCLEAN1979 because of missing means and standard deviations and also because of the procedure used for replacing drop outs, nor from GALLAGHER1983 where dropouts were also replaced.

**Figure 4.6: BT compared with CBT**




Data on effectiveness were extractable from the other studies (see Figure 4.6) and show that BT is at least as effective as CBT as effective as CBT (HRSD: N=3; n = 164; SMD = -0.14 95% CI -0.45, 0.17; BDI: N= 3, n =169; SMD = -0.16 95% CI -0.46, 0.14]) at end of treatment. The effect may be maintained at 6-month follow-up (HRSD: N=1; n = 97; SMD = 0.04 95% CI -0.36, 0.44; BDI: N= 1; n=97; SMD [random effects] = -0.13 95% CI -0.30, 0.04). In an inpatient population all taking antidepressants, it is also more effective than supportive therapy (BDI: N=1; n=25; SMD = -0.69 95% CI -1.52, 0.14)[10], although this is evidence from only one small trial (HOPKO2003). This potential advantage of behavioural activation in more depressed patients is suggested by the subset of patients with severe depression in the DIMAIDJIAN2006 trial where there was a clinically and statistically significant advantage for behavioural activation over CBT (HRSD: SMD = -0.37 95% CI -1.05, 0.31; BDI: SMD = -0.67 95% CI -1.37, 0.02]); this finding was not replicated with moderately depressed patients (HRSD: SMD = 0.12 95% CI -0.61, 0.85; BDI: SMD = 0.24 95% CI -0.49, 0.98). It also appears be as

[10] There is no HRSD data.

effective as antidepressants (HRSD: N=1, n = 78; SMD = -0.12 95% CI -0.58, 0.34), (DIMAIDJIAN2006)

**Summary of the effectiveness of behaviour therapy**

The data set of trials of BT is small and therefore caution should be exercised in the interpretation of this data. However, in the two larger and well conducted trials BT looked as effective, or in the case of severe depression, possibly more effective than CBT. As both these studies focused on the behavioural component of CBT it could be argued that BT may be a simpler treatment to deliver focused primarily on behavioural activation and not requiring more complex interventions directed at changing cognitions. This may also lead to a reduction in the complexity of training with potential implications for uptake in the NHS. However it should be noted that in both trials comparing behavioural activation with CBT, the duration of treatment was the same. In contrast the intervention by HOPKO2003 was explicitly developed as a brief treatment, which may support more simple implementation and training strategies.

### 4.7 Interpersonal psychotherapy

Of the 107 studies identified from searches of electronic databases for IPT, 15 appeared to be relevant RCTs, with seven eventually satisfying the inclusion criteria (DEMELLO2001, ELKIN1989, FRANK1990, REYNOLDS1999, REYNOLDS1999b, SCHULBERG1996, WEISSMAN1992), and eight excluded (DIMASCIO1979, FRANK1989, JACOBSON1977, KLERMAN1974, MARTIN2001, MOSSEY1996, SZAPOCZNIC1982, ZEISS1979). In addition, one unpublished trial (FREEMAN) was obtained from the authors. No additional trials were found from other sources, including searches of reference lists.

The studies recruited patients from a variety of settings, including outpatient and primary care. Most were undertaken in the US, but one was Brazilian (DEMELLO2001) and another British (FREEMAN). Two studies looked at older adults, and in one, most participants had dysthymia as well as major depressive disorder (DEMELLO2001) rather than major depression alone. Four studies looked at the impact of IPT in maintaining the gains of acute phase treatment (REYNOLDS1999, SCHULBERG1996, FRANK1990 and REYNOLDS1999B).

**Comparison 1: IPT compared with placebo (plus clinical management) or usual GP care**

The two trials in this comparison indicate that IPT is more effective than placebo plus clinical management (ELKIN1989) or usual GP care (SCHULBERG1996 - the majority of patients in this arm of the trials received antidepressants). There was a likely clinically significant difference favouring IPT over placebo plus clinical management at the end of treatment on depressive symptoms (HRSD: N = 1, n = 123; SMD = -0.43; 95% CI, -0.79 to -0.07) and on remission (HRSD: N = 1, n = 123; RR = 0.73; 95% CI, 0.56 to 0.93). The same outcomes on the BDI were in the same direction but the effect size for the continuous data was smaller. This difference in strength of effect was also evident for the comparison with usual GP care at the end of treatment on depressive symptoms (BDI: N = 1, n = 72; SMD = -0.69; 95% CI, -1.22 to -0.16; HRSD: N = 1, n = 185; SMD = -0.35; 95% CI, -0.65 to -0.06).

In the comparisons of IPT there was contradictory evidence about the acceptability of IPT to patients (as measured by the likelihood of leaving treatment early). For IPT compared with usual GP care (N = 1, n = 185; RR = 4.14; 95% CI, 2.29 to 7.47) there was a higher attrition rate for IPT but not when IPT was compared with placebo plus clinical management (N = 1, n = 123; RR = 0.57; 95% CI, 0.33 to 0.99).

**Comparison 2: IPT compared with antidepressants**

When IPT is compared with antidepressants the evidence suggests that there is no clinically significant difference between IPT and antidepressants on reducing depressive symptoms at the end of treatment (HRSD: N = 2; n = 302; SMD = 0.08; 95% CI, -0.15 to 0.30). There was also no difference in tolerability between IPT and antidepressants (N = 3, n = 344; RR = 0.94; 95% CI, 0.72 to 1.22). This is contrasts with CBT, which was associated with increased retention in treatment.

**Comparison 3: IPT combined with antidepressants**

The data set on the combination of IPT with antidepressants is very limited but does indicate some advantage over treatment with antidepressants alone on remission at the

end of treatment (HRSD: N = 1, n = 33; RR = 2.26; 95% CI, 1.03 to 4.97) but not on depressive symptoms at 12 weeks (BDI: N = 1, n = 24; SMD = 0.01; 95% CI -0.82 to 0.79). There was insufficient evidence to determine whether IPT combined with antidepressants was more acceptable to patients than antidepressants alone (N= 2, n = 76; RR = 0.39; 95% CI 0.06 to 2.49).

**Comparison 4: IPT as a continuation treatment**

There was some evidence to suggest that IPT may have value as a continuation treatment compared with treatment as usual (TAU), on increasing the likelihood of achieving remission at 4 months (HRSD: N = 1, n = 185; RR = 0.66; 95% CI, 0.53 to 0.82) and in reducing depressive symptoms (HRSD: N = 1, n = 185; SMD = -0.44; 95% CI, -0.73 to -0.15). The limited evidence would also suggest that there is no clinically significant difference between IPT and antidepressants on reducing depressive symptoms at 4 months (HRSD: N = 1, n = 184; SMD = 0.03; 95% CI, -0.26 to 0.32).

IPT in combination with antidepressants also may be effective as a maintenance treatment in preventing relapse at 3 years with a potentially clinically important difference favouring IPT plus antidepressants over antidepressants alone (N = 2, n = 106; RR = 0.62; 95% CI, 0.38 to1.02), but IPT alone does not seem more effective as a maintenance treatment at 3 years compared with antidepressants alone (N = 1, n = 54; RR = 1.29; 95% CI, 0.84 to 1.99). The value of adding antidepressants to IPT is confirmed by the finding of a clinically significant difference favouring IPT plus antidepressants over IPT alone (N = 1, n = 51; RR = 1.73; 95% CI, 1 to 2.98). There was no other evidence to determine the efficacy of IPT against other comparator treatments apart from that covered in the section on CBT above.

**Summary of the effectiveness of IPT**

IPT has been the subject of a small number of RCTs. There is evidence to suggest that IPT is more effective than placebo and usual GP care. In contrast to CBT, IPT in combination with antidepressants does not seem to be a more effective treatment than IPT alone. There is very limited data on the longer-term outcomes on IPT in contrast with CBT. However, it may have some value as a continuation treatment alone or in combination with antidepressants. Given this limited data set, the best evidence for IPT is its equivalence to CBT identified in the previous section on CBT.

### 4.8 Problem solving therapy (PST)

Of the 188 studies initially identified from searches of electronic databases, 12 RCTs were initially identified, with three eventually satisfying the inclusion criteria (DOWRICK2000, MYNORS-WALLIS1995, MYNORS-WALLIS2000), and nine excluded. No additional trials were found from other sources, including searches of reference lists. The studies included a total of 668 patients and include patients from primary care (MYNORS-WALLIS1995, MYNORS-WALLIS2000) or in the case of DOWRICK2000 primary care patients who were recruited by response to a survey in a multi-centre international trial. Comparisons included a "no treatment" control (DOWRICK2000), medication and placebo (MYNORS-WALLIS1995) or medication plus problem solving (MYNORS-WALLIS2000). Problem solving in all three trials involved six sessions over a period of 3 months.

**Comparison 1: Problem solving compared with placebo/no treatment**

There was some evidence to suggest a clinically important difference favouring problem solving over placebo in reducing depressive symptoms by the end of treatment (HRSD: N = 1, n = 55; SMD = -0.69; 95% CI, -1.24 to -0.14; BDI: N = 1, n = 55; SMD = -0.66; 95% CI, -1.24 to -0.14). Problem solving also seemed to have some advantage on improved remission rates at the end of treatment (HRSD: N = 1, n = 60; RR = 0.55; 95% CI, 0.33 to 0.89; BDI: N = 1, n = 60; RR = 0.62; 95% CI, 0.39 to 0.99). However, the effects of problem solving may be not be maintained as there was no evidence of a clinically or statistically significant difference at 6 months after the start of treatment on remission (N = 1, n = 245; RR = 0.83; 95% CI, 0.68 to 1.02) or 12 months after the start of treatment (N = 1, n = 245; RR = 0.98; 95% CI, 0.79 to 1.22). The limited data available on acceptability suggested that problem solving seemed more likely to retain people in treatment than placebo (N = 1, n = 60; RR = 0.11; 95% CI, 0.03 to 0.44).

**Comparison 2: Problem-solving compared with antidepressants**

There is insufficient evidence to determine whether there was a clinically significant difference between problem solving and antidepressants at the end of treatment on depressive symptoms (HRSD: N = 2, n = 124; SMD = 0.10; 95% CI, -0.25 to 0.45; BDI: N = 2, n = 124; SMD = -0.11; 95% CI, -0.46 to 0.25). Similarly evidence from remission data did not suggest a statistically clinical benefit (HRSD: N = 1, n = 116; RR = 1.43; 95% CI, 0.85 to 2.39; BDI: N = 1, n = 61; RR = 0.67; 95% CI, 0.41 to 1.09) nor

were any differences apparent at 12 months after the end of treatment (HRSD: N = 1: n = 116; RR = 0.93; 95% CI, 0.59 to 1.45). There was some evidence to suggest that problem solving compared with antidepressants may be associated with increased acceptability of treatment including leaving treatment early for any reason (N = 2, n = 177; RR [random effects] = 0.88; 95% CI, 0.18 to 4.2) and leaving treatment due to side effects (N = 2, n = 177; RR = 0.12; 95% CI, 0.01 to 0.97).

However, the addition of problem solving to antidepressants seems to confer no clinical benefits on the provision of antidepressants alone in increasing the likelihood of remission by the end of treatment (HRSD: N = 1, n = 71; RR = 1.2; 95% CI,0.65 to 2.22) or reducing depressive symptoms at the end of treatment (HRSD: N = 1, n = 65; SMD = 0.35; 95% CI, -0.14 to 0.84; BDI: N = 1, n = 65; SMD = -0.37; 95% CI, -0.86 to 0.12). This also holds for 1 year after the end of treatment where there was no significant difference between problem solving plus antidepressants and antidepressants alone on achieving remission (HRSD: N = 1, n = 71; RR = 0.77; 95% CI, 0.43 to 1.39).

**Summary of the effectiveness of problem solving**

There is limited evidence from a small number of trials for the efficacy of problem solving. There is no data on the long-term benefits of problem-solving but in contrast with the other treatments so far reviewed it is a brief treatment and so it might be expected that long-term benefits may not be obtained. Also in contrast with CBT, and to a lesser extent IPT, it does not appear to have any additional benefits when combined with antidepressants compared with IPT alone. Again, this may be due to the short-term nature of the intervention but also because it has generally been provided for a primary care population who would be expected to present with milder and less chronic depression than those in trials based in secondary care.

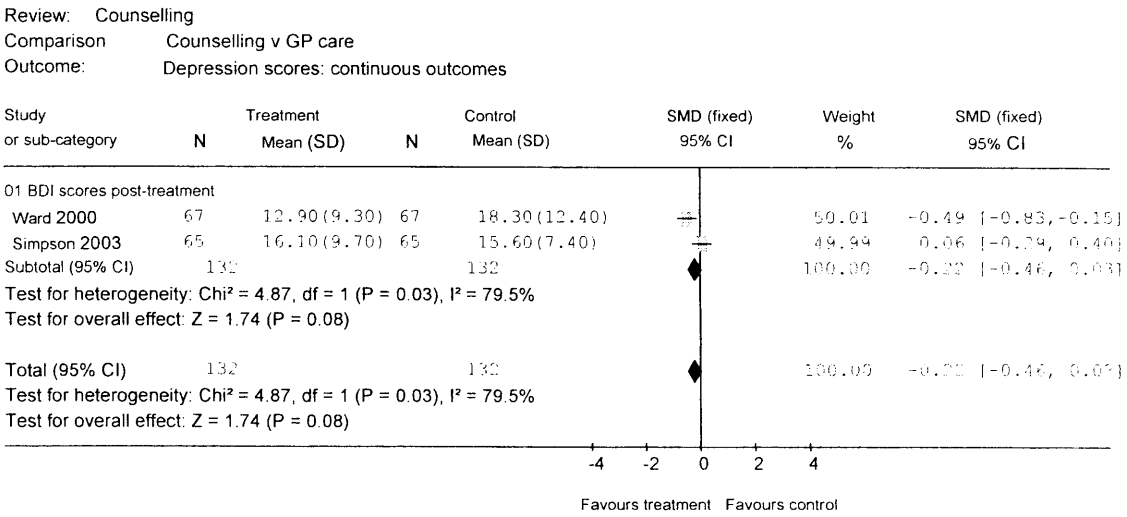
### 4.9 Counselling

Of the 1,027 references originally identified from searches of electronic databases, nine appeared to be relevant RCTs, with three eventually satisfying the inclusion criteria and six excluded. No additional trials were found from other sources, including searches of reference lists. The three included studies (BEDI2000, SIMPSON2003 and WARD2000) were all conducted in primary care settings in the UK and included a total of 712 patients. In BEDI2000 the comparator treatment was antidepressant medication

and in SIMPSON2003 the comparison was treatment as usual. In SIMPSON2003 between 30% to 40% of patients in both groups were prescribed antidepressants at various points in the study. In WARD2000 only 62% had a diagnosis of depression but all participants had a BDI score of 14 or over. It was included due to limited data in this section. The comparator treatments were CBT and usual GP care. In addition, despite GPs being asked not to prescribe antidepressants for study, 30% of the counselling group and 27% of those receiving CBT were prescribed antidepressants. BEDI2000 offered just six sessions of therapy but WARD2000 and SIMPSON2003 offered between six and 12 sessions.

When compared with GP/usual care (see Figure 4.7), counselling did not appear to be clinically effective at 4 to 6 months after starting treatment (BDI: N = 2, n = 132; SMD [random effects] = -0.22; 95% CI, -0.75 to 0.32). This analysis had significant heterogeneity and may reflect the fact that SIMPSON2003 included patients with chronic depression while WARD2000 only included 62% of patients with a diagnosis of depression. When compared with antidepressants, there was no clinically or statistically significant differences at end of treatment on depressive symptoms (BDI: N = 1, n = 83; SMD = 0.04; 95% CI, -0.39, 0.47) or an RDC score greater than 3 (N = 1, n = 103; RR = 1.20; 95% CI = 0.80 to 1.80) but at 12-month follow-up antidepressants were clinically and statistically more effective on RDC score greater than 3 (N= 1, n = 103; RR = 1.41; 95% CI, 1.08 to 1.83).

**Figure 4.7: Counselling versus usual care**



There was no data in BEDI 2000 to determine if counselling was more tolerable than antidepressants and insufficient evidence to determine whether there is a clinically significant difference between counselling and GP care on reducing the likelihood of patients leaving the study early 4 months after the start of treatment (N = 1, n = 134; RR = 1.00; 95% CI, 0.30 to 3.30) or 12 months after the start of treatment (N = 1, n = 134; RR = 0.90; 95% CI, 0.39 to 2.07).

**Summary of the effectiveness of counselling**

Given that counselling is the most widely available intervention in the NHS for common mental disorders in primary care (Mellor-Clark *et al.*, 2001) the results of this analysis are disappointing as they do not indicate a clear clinically significant effect for counselling; it appears to be as effective as antidepressants at end of treatment in one study but at 12 months antidepressants appear to be more effective. In addition, at the end of treatment counselling does not appear to be more effective than usual care. In contrast with other treatments it does not appear to be associated with greater tolerability. The results are also at odds with Cape and colleagues (2007), quoted at the beginning of this chapter, who obtained a small but perhaps not clinically significant effect (n = 766; SMD = -0.29; 95% CI -0.44, -0.14). However, the studies analysed by Cape and colleagues (2007) included a significant number of non-depressed patients. This finding is replicated to some extent in this analysis, as the one study with consistent positive results (WARD2000) included a significant number of patients (38%) who did not have a primary diagnosis of depression.

### 4.10 Short-term psychodynamic psychotherapy (STPP)

Of the 188 references identified in the initial search of electronic databases, 11 appeared to be relevant RCTs, with three eventually satisfying the inclusion criteria (GALLAGHER-THOMPSON1994, MCLEAN1979, SHAPIRO1994), and eight excluded. An additional trial (BURNAND2002) was identified through an update search. No further trials were found from other sources, including searches of reference lists. The four trials included a total of 432 patients, although efficacy data was not used from MCCLEAN1979 because of the procedure used for replacing patients who dropped out of the study. Comparisons included psychotherapy plus antidepressants versus antidepressants alone (BURNAND2002), psychotherapy versus CBT

(GALLAGHER-THOMPSON1994, SHAPIRO1994) and psychotherapy versus BT and antidepressants (MCCLEAN1979). There were no comparisons against wait list or treatment as usual. Treatment took place in outpatient settings and varied between 10 to 20 sessions over a 10 to 16 week period.

There was no evidence of a clinically significant difference between psychodynamic psychotherapy and CBT on reducing depressive symptoms at the end of treatment (BDI: N = 3, n = 57; SMD [random effects] = 0.35; 95% CI, -0.61 to 1.30), at 6 months after treatment (BDI: N = 3, n = 56; SMD = -0.13; 95% CI, -0.40 to 0.67) or at 1 year after treatment (BDI: N = 3, n = 50; SMD [random effects] = -0.22; 95% CI, -1.22 to 0.79). In a separate study there was no evidence of a significant difference on reducing the likelihood of still being depressed at the end of treatment as measured by RDC criteria (N = 1, n = 66; RR = 1.7; 95% CI, 0.97 to 2.97) or 3 months after treatment (N = 1, n = 66; RR = 1.34; 95% CI, 0.86 to 2.08). The addition of psychotherapy to antidepressants compared with antidepressants and supportive therapy did not appear to bring additional clinically important benefits on remission at the end of treatment (N = 1, n = 95; RR = 1.09; 95% CI, 0.8 to 1.48) or on reducing depressive symptoms by the end of treatment (N = 1, n = 74; SMD = -0.11; 95% CI, -0.57 to 0.35).

There was some evidence to suggest a clinically significant difference favouring BT over psychodynamic therapy on reducing the likelihood of leaving treatment early (N = 1, n = 95; RR = 3.02; 95% CI, 1.07 to 8.5). No other examples of this comparison achieve significance although in most studies there is a trend favoring the comparator over STPP when it comes to retaining people in treatment. This can be seen in the comparison between psychodynamic treatment and antidepressants (N = 1, n = 90; RR = 0.76; 95% CI, 0.41 to 1.41), psychodynamic psychotherapy and CBT (N = 1, n = 66; RR = 2.16; 95% CI, 0.81 to 5.76) and psychodynamic psychotherapy plus antidepressants and antidepressants plus supportive therapy (N = 1, n = 95; RR = 1.43; 95% CI, 0.71 to 2.89).

**Summary of the effectiveness of short-term psychodynamic psychotherapy**

The evidence base for STPP is limited and it is difficult to draw any firm conclusions; in one trial there seems broad equivalence with CBT but some suggestion of a potential advantage for CBT in another trial. As with problem solving, the addition of STPP to

antidepressants did not produce any clear advantage over STPP alone. Perhaps the most consistent finding across all trials is for a modest increased drop-out rate associated with STPP.

### 4.11 Short-term psychological treatments

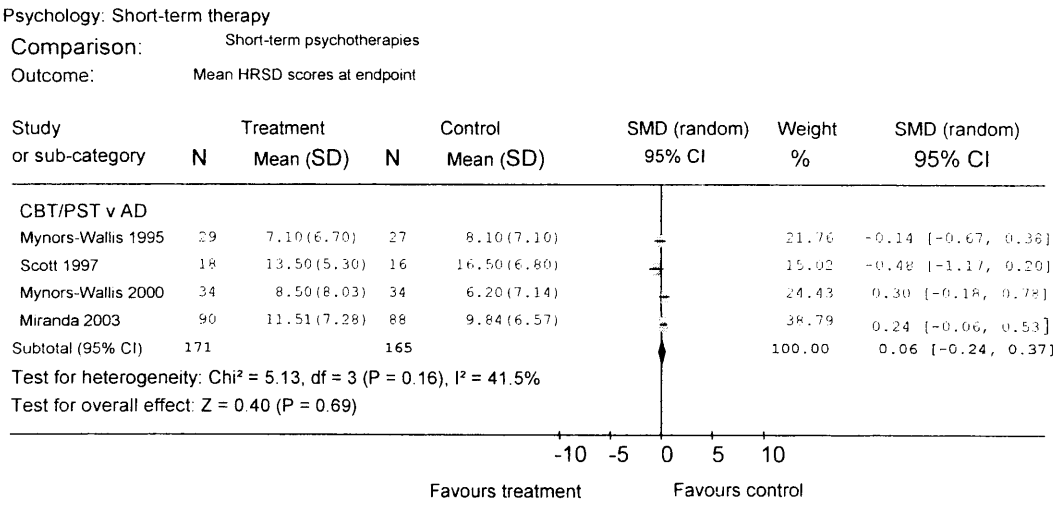
In primary care in the UK there is a strong tradition of providing brief interventions for common mental health problems, often delivered by counsellors (Mellor-Clark *et al.*, 2001). However, as can be seen from the analyses above, the evidence for counselling is limited. The question remains, particularly in primary care and in relation to collaborative care, whether it is possible to obtain any significant effects for brief treatments for depression. This has potentially significant implications for collaborative care where the interventions provided (for example, by depression care specialists) have tended to be brief (see Chapter 2).

A review of the psychological interventions considered so far indicates that evidence for efficacy is of reasonable quality for CBT and to a lesser extent for IPT, BT and problem solving, but that the evidence for counselling and short-term psychodynamic therapy is weaker. For the purpose of this review short-term treatments were defined as those offering between six and 12 sessions of treatment. Unfortunately no direct comparison of short versus standard treatment was available within the current data set. A review of all the trials reviewed in the four effective treatments identified six trials which offered short-term treatment. Four of these trials were based in primary care and included comparisons against antidepressants (MIRANDA2003 [CBT versus antidepressants], MYNORS-WALLIS1995 [problem solving therapy versus antidepressants], MYNORS-WALLIS2000 [problem solving therapy versus antidepressants] and SCOTT1997 [CBT versus GP care, with all but one of the participants on antidepressants]). Two other studies (SELMI1990 [CBT versus wait list control] and HOPKO2003 [BT versus standard care in an inpatient setting]) also offered brief treatments but were excluded for further consideration as wait list is a weak comparator and inpatients were considered an atypical group especially when considering collaborative care. Three studies delivered six sessions (MYNORS-WALLIS1995, MYNORS-WALLIS2000, SCOTT1997) and one delivered eight sessions (MIRANDA2003).

**Short-term psychological treatments versus antidepressants**

In the comparison with antidepressants there was no evidence of any statistical or clinically significant difference between short-term treatments and antidepressants on depressive symptoms at the end of treatment (HRSD: N = 4, n= 336; SMD [random effects] = 0.06; 95% CI, -0.24 to 0.37) and no evidence of a statistical or clinically significant effect on remission at 1-year follow-up on short-term treatments versus antidepressants (HRSD: N = 2, n = 294; RR = 0.86; 95% CI, 0.66 to 1.12) (see Figure 4.8).

**Figure 4.8: Short-term interventions versus antidepressants**




There was also insufficient evidence to determine if there was a clinically significant difference between short-term psychological therapies and antidepressants on reducing the likelihood of leaving treatment early for any reason (N = 3, n = 225; RR = 1.20; 95% CI, 0.70 to 2.07). There is some evidence suggesting that there is a clinically significant difference favouring short-term psychological therapies over other treatments on reducing the likelihood of leaving treatment early due to side effects (N= 2, n= 177; RR= 0.12; 95% CI, 0.01 to 0.97).

**Summary of the effectiveness of short-term psychological treatments**

The evidence for short-term psychological therapies (problem solving therapy or CBT) is limited but suggests that in primary care or community settings they may be as effective as antidepressants and that they may also be as effective as antidepressants at follow-up. Short-term psychological treatments also seem to be more acceptable than

antidepressants. However, it should be noted that this is a limited data set but one that does have some direct relevance to collaborative care given its predominantly primary care focus. Both brief CBT and PST were developed specifically for use in the treatment of depression and developed specifically for use in primary care (problem solving) or adapted for use in primary care or community settings (MIRANDA2003, SCOTT1997).

### 4.12 Guided self-help (GSH)

The above review suggests that short-term treatments may have some benefit for the treatment of depression. Another way of providing brief or more attenuated forms of treatments is through various forms of self-help in which the patient essentially self-administers the treatment. The interest in this model of treatment lies in its potential increased cost effectiveness and more effective use of professional resources. It can take two forms: pure self-help, in which the patient receives no input from a professional or para-professional and may simply be directed to use the treatment; and guided self-help (GSH), where the patient is primarily responsible for the self-administration of the treatment but receives help and advice from a professional. (Computer assisted self-help has been developed more recently [for example, NICE, 2006].) The broad trend has been for pure self-help to be delivered more for anxiety disorders and guided self-help programmes to be provided more for depression or for mixed anxiety and depression (Cuijpers *et al.*, 1997; Lewis *et al.*, 2003; Gellaty *et al.*, 2007).

As this review is concerned with the treatment of depression, and in particular its application to collaborative care, the focus will be on guided self-help. This is consistent with the review by Lewis and colleagues (2003) that supported the use of guided self-help, based on CBT principles. A meta-analysis by Cuijpers (1997) of a small number of low-quality studies also suggested that guided self-help for depression may be no less effective than individual or group therapy (at 6-month follow up). As computer programmes for the treatment of depression were not widely available in the NHS at the start of the review this form of guided self-help will not be considered.

A large number of self-help guides for depression exist, the large majority of which have not been subject to formal evaluation (Anderson *et al.*, 2005). However, in order to identify relevant trials, the review was limited to guided self-help programmes based on

evidence-based interventions for depression as discussed in the review so far. Specifically, guided self-help programmes for depression were defined as a self-administered intervention designed to treat depression, which makes use of a range of books or a self-help manual that is based on an evidence-based intervention and designed specifically for the purpose. A healthcare professional (or para-professional) facilitates the use of this material by introducing, monitoring and reviewing the outcome of such treatment.

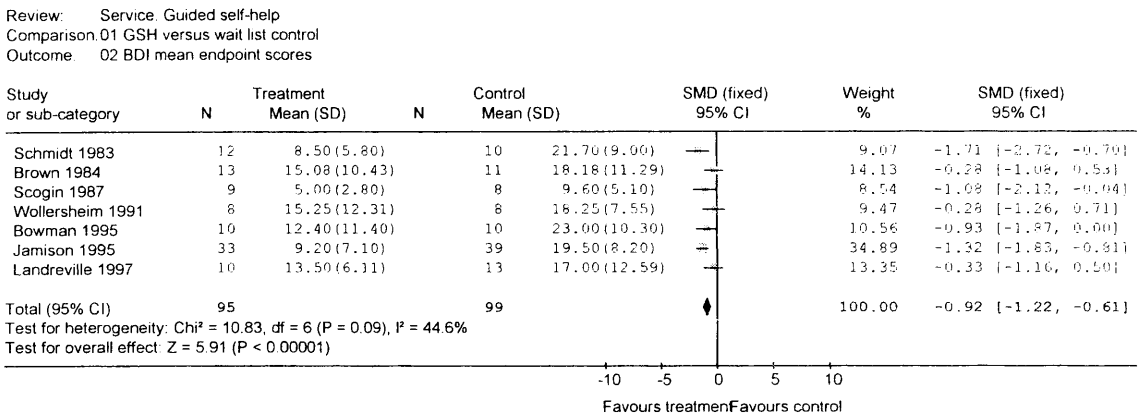
Nine RCTs of guided self-help interventions used in the treatment and management of depression were identified from the search of electronic databases (BEUTLER1991, BOWMAN1995, BROWN1984, JAMISON1995, LANDREVILLE1997, SCHMIDT1983, SCOGIN1987, SCOGIN1989, WOLLERSHEIM1991) and one trial identified from reference lists (FLOYD2004), providing data on 484 participants. Fourteen studies were excluded (see Appendix I). The comparisons included guided self-help with wait list control, individual and group CBT, group guided self-help, telephone contact and individual or group psychotherapy. All guided self-help materials used were based on either CBT or BT principles.

*Comparison 1: Guided self-help versus wait list control*

There was good evidence of a clinically significant difference favouring guided self-help over wait list control at the end of treatment on achieving remission (defined as BDI≤11) (N = 2, n = 96; RR = 0.60; 95% CI, 0.44 to 0.80), and in reducing depressive symptoms as measured by the BDI (N = 7, n = 194; SMD = -0.92; 95% CI, -1.22 to –0.61) and the HRSD (N = 4, n = 151; SMD = -1.60; 95% CI, -1.1.98 to –1.23) (see

Figure 4.9)

**Figure 4.9: Guided self-help versus wait list**




## Comparison 2: Guided self-help versus individual psychological therapy

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and individual psychological therapies on reducing depressive symptoms at the end of treatment (BDI: N = 2, n = 47; SMD = 0.20; 95% CI, -0.37 to 0.78) and at 10-month follow-up (BDI: N = 2, n = 39; SMD = -0.10; 95% CI, -0.73 to 0.53). On the HRSD there was no difference between guided self-help and another non-depression specific individual therapy (self-examination therapy) (N = 1, n = 20; SMD = 0.1 (-0.78, 0.97). There was also no evidence of a statistically significant difference on leaving the study early but there was a trend favouring self-help (N= 3, n=76; RR = 0.60; 95% CI, 0.25 to 1.46).

**Summary of the effectiveness of guided self-help**

Guided self-help produces a clinically significant reduction in depressive symptoms when compared with wait list control although that is not a very stringent test of clinical efficacy. More important is the equivalence against a range of individual and group treatments. There are no comparisons against treatment as usual or antidepressant medication both of which might allow for a more informative comparison against other interventions covered in this review. Nevertheless there is some evidence of efficacy and some suggestion that these outcomes might not all be short-term. However, it should be noted that the populations involved were often recruited via adverts and tended to have mild depression; for example, baseline scores in FLOYD2004 were below 17.5 on the HRSD in all three conditions and in SCOGIN1987 patients had to have a diagnosis of depression and a BDI score above 10. This would suggest that the treatment may be best suited to people with mild depression.

The outcomes of this review are broadly in line with that of the reviews of Gellaty and colleagues (2007) and Lewis and colleagues (2003) although both these reviews were concerned with guided self-help in depression and anxiety. Both identified cognitive behavioral principles as being important and Gellaty and colleagues (2007) suggest that more significant effects may be seen when all patients in the study meet full diagnostic criteria for depression and where the intervention was provided by non-professionals. The range and nature of the interventions varied considerably in this review and therefore it is not surprising that Gellaty and colleagues (2007) were unable to identify any specific mode of delivery of guided self-help that was associated with more favourable outcomes, such as the number of sessions. Guided self-help has obvious limitations such as a requirement of a certain reading ability, and understanding of the language used; for example, 22% of the USA population is functionally illiterate, and 44% will not read a book in any year (National Center for Education Statistics, 1997).

**4.12 Overall summary of the effectiveness of psychological interventions**

This review has demonstrated that psychological interventions are effective treatments for depression and this is consistent with the findings of previous reviews (for example, Gloaguen *et al.*, 1998; Pampallona *et al.*, 2004; Roth & Fonagy, 2005). Effective interventions tend to be those specifically designed for depression (for example, CBT, BT or IPT) but the effects are modest and in many cases the evidence for long-term

efficacy is largely absent except for the limited data on CBT. There is some evidence that brief interventions based on CBT principles (such as brief CBT or problem solving) can be as effective as antidepressants but the data on long-term efficacy are limited. Finally the use of guided self-help appears to have some benefits—at least for milder depression—but the knowledge of its long-term effects is limited. These brief interventions, often collectively referred to as "low intensity" interventions (Roth & Pilling, 2007a) may potentially play an important role in the delivery of collaborative care.

In relation to the provision of psychological interventions by case managers or primary care mental health workers (PCMHWs) as part of a collaborative care intervention, the evidence suggests that two options might be considered. They are the provision of attenuated forms of effective treatments such as brief CBT, brief BT, or problem solving, or guided self-help delivered by para-professionals working in primary care. Secondly, the provision of standard CBT or IPT by mental health specialists as part of a stepped care approach within a collaborative care programme (for example, Hunkeler *et al.*, 2002; Bruce *et al.*, 2004) is suggested by the evidence reviewed above.

### 4.13 Factors influencing the effectiveness of psychological therapies

The rest of this chapter will be concerned with a review of a number of additional factors that should be considered in identifying the psychological treatment approaches compatible with an effective collaborative care service based in primary care. These factors include the non-specific or common factors associated with treatment outcome, including the therapeutic alliance, therapist factors and factors associated with variability in the delivery of psychological interventions, such as the competences required to deliver effective treatment. Unfortunately, the evidence in these areas is limited and identifying the "active ingredients" in effective psychological treatment is difficult. These difficulties relate to both the therapies themselves and other factors, including the nature of the disorder being treated.

Although separate psychological treatment approaches can be operationalised into "pure forms", in practice most psychological treatments for depression share common features. Indeed, there has been long debate about the "specificity versus the non-specificity" of treatment (Karasu, 1986; Roth & Fonagy, 2005). Many of these common

features relate to the therapeutic relationship, such as an accepting, open and active listening relationship. There have also been proposals for an integration of psychological therapies (Norcross & Goldfried, 1992; Wampold *et al.*, 2002). An alternative approach, such as that developed by Jacobson and colleagues (1996), has been to try to identify the mutative components of particular therapies, focusing in their case on behavioural activation in CBT (see above). Others have suggested that commonalties between CBT and IPT may be explained by the common emphasis on structured homework and a focus on cognitions, which are essentially key components of CBT (Albon & Jones, 2002). Alternatives to this approach have focused on integration, including developments in cognitive behavioural treatments which seek to integrate cognitive and developmental approaches in the treatment of depression (Keller *et al.*, 2000) or the cognitive and the psychodynamic, such as in cognitive analytic therapy (Ryle, 1989). Following the review above, the adoption of this approach might argue for identifying the common elements across the range of effective treatments, which might suggest a structured activity-focused approach that draws on elements from CBT, BT and problem solving. However there is, as yet, little evidence to support such an approach (Roth & Fonagy, 2005).

Independently of whether or not an integrationist approach to psychological treatment may be appropriate, non-specific factors such as therapist variables, patient variables and the therapeutic alliance can influence the outcome of treatment and they are therefore briefly reviewed below with a particular emphasis on the implications for the use of psychological interventions in collaborative care.

### 4.14 Patient factors

In a number of the critiques of RCTs of psychological therapies, a central concern has been the unrepresentativeness of the patient population in clinical trials (for example, Shadish *et al.*, 2000). However, as has been argued in Chapter 2 this criticism may well be overstated. Perhaps the more significant identifiable patient variable is the severity of depression, given the evidence from the review above of differential effects of patients with different severities of depression. There is also evidence that the effectiveness of psychotherapy designed for depression can vary across individuals (Sotsky *et al.*, 1991) and these may affect the rate at which people respond to treatment (Hardy *et al.*, 2001).

There is some evidence that patients who are perfectionistic (Blatt *et al.*, 1996a) and highly self-critical (Rector *et al.*, 2000) may do less well with standardised therapies. However, the studies in the review above and other reviews do not control for these variables (they are very rarely reported in clinical trials) and they are not easy to identify without significant resources, including primary research. Factors which may more easily be taken into account include the severity of depression, the impact of socioeconomic factors (for example, poverty and unemployment) on the course of depression and the effects of previous treatment. A consideration of the evidence above suggests that brief interventions may have a place in the treatment of depression but that their use in combination with antidepressants for more moderate or severe depression is unclear. The evidence would also suggest that for improved long-term outcomes (particularly for people with previous episodes of depression) standard or long-term treatments may be needed. It suggests that services should have the flexibility to provide long-term treatments for those with more severe depression and that one of the roles of PCMHWs or others might be in facilitating access to such interventions.

### 4.15 Therapist factors

It is accepted that in routine practice there is often considerable attenuation of the effects seen in clinical trials but the reasons for this are not well understood (Shadish *et al.*, 2000). This is not surprising since controlled trials are designed to reduce variation which might arise from difference in therapist performance. However, even in clinical trials variation in therapist performance is apparent (Shaw *et al.*, 1999). While the extent of this variation is uncertain, indications from meta-analyses of controlled trials and effectiveness studies indicate that differences in outcome can be considerable, in some cases varying by over 100% between best and worst performing therapist (Brown *et al.*, 2005; Okiishi *et al.*, 2003). Reviews of clinical trials suggest that there is considerable variation in the experience and training associated with those delivering the interventions but evidence concerning the levels of competence or skill required to guarantee certain outcomes is more difficult to obtain (Roth & Pilling, 2007b). What is clear is that most trials provide effective supervision and this may be an important factor in improving the outcomes of clinical trials, but again the evidence for this is limited (Cape & Barkham, 2002; Roth & Pilling, 2007b). This is of particular importance in collaborative care, as supervision as been identified in the meta-

regressions as a variable associated with positive outcomes (for example, Gilbody *et al.*, 2006a). This suggests that specifying and determining the competence of individuals providing low-intensity brief interventions, particularly where the treatment manuals are often not as well developed as for standard treatments, is of considerable importance. This will be a particular focus of Chapter 5.

**The therapeutic alliance**

Some have argued that the therapeutic alliance is the central mediator of change in all psychological therapies and it is the key "non-specific" factor carrying much of the variance in outcome (Ahn & Wampold, 2001). There has also been a long tradition of measuring the alliance and linking this to outcome (for example, Luborsky *et al.*, 1975). This has been the subject of a number of recent reviews (for example, Horvath, 2000; Martin *et al.*, 2000), which have demonstrated that the alliance is associated with positive outcomes, but that the correlation is consistent but relatively low (0.25 in the case of Martin *et al.* [2000]). Two factors deserve consideration in relation to the development of a psychological intervention in collaborative care: first how the therapeutic alliance may be established in brief structured interventions of the kind delivered in collaborative care; and secondly, the aspects of the interventions that may be associated with the promotion of the alliance. Indeed, there have been important developments in understanding the role of the therapeutic relationship and alliance (Safran & Muran, 2000) and therapeutic 'universals', such as remoralisation, social support and reassurance, are also regarded as important factors for treatments (Norcross, 2002; Schaap *et al.*, 1993). The importance of these factors in developing a collaborative care intervention will be considered in Chapters 5 and 6.

**Limitations of the review**

This chapter was concerned with the evaluation of psychological interventions for the treatment of depression with particular emphasis on their application to collaborative care. While the review has identified a number of possible options for the psychological treatment of depression it suffers from a number of limitations.

First, in common with the pharmacological treatment of depression, there may be a publication bias resulting in negative trials not being published. Unfortunately, with the exception of the data set on CBT, there are too few trials to formally check if this is the

case (there was no evidence of publication bias in the funnel plots for the CBT studies). Secondly, the data suffers from a limited data set on remission and a lack of long-term outcomes, with limited data in these two areas only available for CBT. In addition, important information about patient populations is limited, with severity the only reasonable measure with which to compare patient groups.

Importantly, there was no substantial evidence on the effectiveness of psychological interventions as part of primary care, of a collaborative care intervention or a stepped care intervention – all of which imposes limitations on the interpretation of the data in relation to a UK-based collaborative care initiative. The trials also provide little information about the competences required to deliver the intervention effectively and this is a considerable concern when para-professionals may be involved in the delivery of the intervention. In a related area there is very little evidence on training required by those delivering the interventions. Finally, the data set are primarily from the US and this also raises a caution about their transition to a UK setting.

# 5. Identifying the Competences to Deliver Brief Effective Psychological Interventions in Collaborative Care

## 5.1 Introduction

In Chapter 4 a number of options were identified for the provision of psychological interventions by PCMHWs, case managers or others as an integral part of a collaborative care intervention. These included a number of low intensity interventions[11] including attenuated forms of effective treatments such as brief CBT or brief BT, problem solving therapy or guided self-help. The provision of standard, that is longer-term, CBT or IPT by mental health specialists may form part of a collaborative care programme, but the role of the PCMHW or case manager would be to facilitate uptake of these interventions rather than to directly provide them. While the systems for supporting the delivery of standard psychological treatments such as CBT and IPT are well developed and include treatment manuals and supervision systems (Roth *et al.*, 2007), those for brief interventions and guided self-help are not so well established (Roth *et al.*, 2007). Having identified in Chapter 4 that therapist competence is a major factor in determining the outcome of psychological interventions (for example, Brown *et al.*, 2005), this is an important issue. It is therefore important that the competences required to deliver brief interventions in collaborative care are clearly specified, and this is the main focus of this chapter.

For low intensity interventions the review in Chapter 4 suggested that brief CBT, brief BT, problem solving and guided self-help based on CBT principles may be the most effective interventions. While the relative effectiveness of an intervention is a key consideration in determining the choice of interventions, additional factors also influence the decision about which interventions to choose. From the perspective of this thesis key considerations include the feasibility of their implementation in routine care and the training and supporting PCMHWs required to ensure their effective

[11] The term "low-intensity intervention" is used here as an overarching term to describe a range of attenuated forms of cognitive and behavioral interventions including behavioural activation and guided self-help.

implementation; that is, interventions that required relatively limited training, did not require a sophisticated assessment or formulation, could be relatively easily specified in treatment protocols, had a good fit with models already adopted in primary care and lent themselves to an efficient use of supervision and support, would be preferred. A consideration of these factors suggests that two interventions would potentially be the most suitable psychological interventions in this context: guided self-help and behavioral activation for depression. Brief CBT was viewed as requiring too much training, particularly for individuals with limited experience of psychological therapies, and the evidence base for problem solving therapy is weaker.

Having identified the possible interventions, the question of training and delivering the interventions in an effective manner then needs to be considered. An increasingly influential way in which this is determined is by specifying what the competences are that are required to deliver the interventions (Roth & Pilling, 2007a).

Although there is a considerable literature on the practice of psychological interventions, and in particular on the process of delivering the interventions, it remains a challenge to specify exactly what an individual should do to conduct them in a competent manner (Roth & Fonagy, 2005). For understandable reasons the conduct of psychological interventions is often described in conceptual as much as behavioural terms. The techniques used by psychological therapists can be seen as methods for helping individuals move from one mental or behavioural state to another, guided by a higher-order model of mental disorder. This means that psychological therapists are oriented by a sense of "why" something is being done, and most treatment models stress the importance of this "procedural knowledge" as a critical part of therapist competence (Bennett-Levy, 2005). However, procedural knowledge is often hard to identify; it may be observable at points when it guides action, but more often it is implicit in the decision-making process that results in the delivery of the competent and skilled behaviours that comprises a successful psychological intervention. Given this difficulty it is not surprising that criteria for the successful delivery of psychological interventions are often expressed in terms of professional standards (for example, the standards set by a training body), rather than by more empirical criteria such as whether a therapist who demonstrates competence has better clinical outcomes than one who does not. This is a

consequence in part of the limited knowledge about the relation between process and outcome in psychological therapy.

Although professional standards are set in the expectation that someone who meets particular training criteria should achieve better outcomes, there is surprisingly little evidence to support this position. A number of reviews have failed to show the benefits of higher levels of training or years of experience (for example, Stein & Lambert, 1995), although other studies have demonstrated the benefits of training in a range of modalities (for example, Crits-Christoph *et al.*, 1998). From the perspective of collaborative care, this matter is further complicated by the fact that low-intensity interventions, which form an important element of many collaborative care interventions, are often delivered by individuals without either a professional training or a formal qualification in a psychological therapy. This suggests that a more useful question to ask might be: what are the competences required to deliver an effective intervention that is associated with a positive outcome? This shifts the focus from accreditation to practice while acknowledging the potential gap between the two. This distinction is widely recognised in other fields; for example, medical (and especially surgical) reporting systems are based on outcomes, and these make it clear that basic training does not always guarantee proficiency (for example, Marshall *et al.*, 2000).

### 5.2 Competence, fidelity and adherence

Before focusing specifically on the competences for low-intensity psychological interventions it may be helpful to clarify a number of relevant terms. These include the terms adherence, fidelity and competence. The first two terms are mostly used by researchers concerned with the formal evaluation of psychological therapies who often monitor "fidelity to treatment", that is the extent to which therapists are delivering the therapy as intended (Waltz *et al.*, 1993). This is usually referred to as adherence and is defined by the extent to which therapists apply the interventions as indicated in the treatment manual, and avoid using procedures proscribed by a manual. Competence is not the same as adherence and simple adherence does not imply competence in its delivery; Waltz and colleagues (1993) define competence as the level of skill shown by the therapist in delivering the treatment. Their conception of skill also encompasses a great deal of what might be seen as clinical judgment, including the therapist's capacity

to conceptualise a client's problems, and to tailor the intervention to the needs of the client. For the purposes of this review, a competent psychological therapist is one who identifies and applies a defined set of knowledge, thought and behaviours (competences) to deliver an intervention in a manner that can be reasonably expected to produce a positive outcome.

It is also important not to confuse experience and training with competence, although they are sometimes taken as proxies for competence, as there is a commonsense expectation that these factors should relate both to practice and to outcome. However, reviews are reasonably consistent, and tend to indicate that at best there is a modest relationship between these variables and at worst no relationship (for example, Lyons & Wood, 1991; Stein & Lambert, 1995). However, it should be borne in mind that few if any trials have set out to examine relationships between these factors directly, and a number of methodological considerations make these findings less concerning than at first might appear. Nonetheless it seems sensible to question the notion that experience and training are simply and directly to therapist competence. For example, there is evidence that training can make therapists more competent (for example, Milne *et al.*, 1999), but within this study it was clear that some therapists showed the benefit more than others; therefore assumption that training invariably leads to competence may not be valid.

The variable findings emerging from the literature on training also serve as a reminder that simply specifying competences does not guarantee positive outcomes. A useful concept here is that of meta-competence (Roth & Pilling, 2007a), which is an overarching capacity to hold in mind the overall structure and objective of an intervention while responding to the particular needs of each individual. Meta-competences may therefore be important in dealing with threats to the therapeutic alliance without deviating completely from the initial therapeutic aims or approaching new problems as they emerge during the course of treatment. The concept of meta-competence has similarities with the model developed by Bennett-Levy (2005), in which he distinguishes between declarative, procedural and reflective knowledge, the latter two covering much of what is contained in the concept of meta-competence.

For some authorities, the emphasis on therapist competence and its focus on the use of particular techniques is of less importance than the therapeutic alliance (Luborsky *et al.*, 1975; Ahn & Wampold, 2001; Stiles *et al.*, 2006). The alliance is seen as the constructive relationship between therapist and client, characterised by a positive and mutually respectful stance in which both parties are oriented towards the joint enterprise of change (Roth & Fonagy, 2005). From a research perspective the alliance is usually conceptualised as having three elements (Bordin, 1979): the relationship between therapist and patient; agreement (whether tacit or explicit) regarding the relevance of the tasks (or techniques) employed in therapy; and agreement about the goals or outcomes the therapy aims to achieve.

While the exact contribution of the alliance to outcome may still be the source of dispute, the findings that it has an association with the outcome of treatment are consistently supported by meta-analytic reviews which indicate a correlation between alliance and outcome of around 0.25 (for example, Horvath & Symonds, 1991; Martin *et al.*, 2000). However, it is the consistency, rather than the size of this correlation, which is most striking, since it accounts for only 6% of the variance in the known outcome[12] On this basis it is reasonable to consider to what extent a good alliance is necessary to achieve a positive outcome, because the alliance, with its low correlation with outcome, cannot be regarded as sufficient. A consideration of the therapeutic alliance has particular importance for collaborative care where its development and maintenance can present a considerable challenge when the interventions are brief and may often be conducted by telephone.

### 5.3 The competences required to deliver psychological interventions in collaborative care

The focus of this chapter is on two low-intensity psychological interventions that were identified as compatible with a collaborative care approach in the treatment of depression. The key competences associated with these interventions are described below. However, before describing these in detail a wider conceptual framework for

[12] It should be noted that in most studies it is not possible to account for more that 30 to 40% of the total variance in outcome (Craighead *et al.*, 2005) so that 6% may account for 15 to 20% of the known variance.

describing the competences for evidence-based psychological therapies, and CBT in particular, is set out below. This framework was developed as part of a broader programme of work on competences in psychological therapies developed by the author and colleagues (Roth & Pilling, 2007a & b; Roth *et al.*, 2007). This element of the work is focused on cognitive and behavioural therapies and includes both CBT (for example, Beck *et al.*, 1979) and BT (for example, Martell *et al.*, 2001).

### 5.4 Developing a CBT competence framework

The purpose behind the framework was to develop a pragmatic approach to improve therapist performance that was compatible with existing practice. It drew on the current evidence base of the psychological therapies (see Chapter 4 for an example of this data set for depression) but was intended to have value for the range of mental disorders. As a consequence it relied heavily on RCTs and the associated treatment manuals and where available the methods and tools used to monitor adherence. These manuals and adherence tools provide a valuable source of information for the development of the framework but they were often not suited to practical use in routine clinical practice and in particular for collaborative care interventions in primary care.

The essential elements of the CBT competence framework (Roth & Pilling, 2007a) are set out below and are compatible with a collaborative care approach. The key building blocks include:

- Location within a stepped care framework.
- A distinction between low- and high-intensity interventions; in this context "high-intensity" denotes a formal psychological therapy delivered by a specialist psychological therapist (such as standard CBT or IPT). Low-intensity interventions are more varied, including, for example, guided self-help or brief interventions that retain a sense of self-help, albeit in the context of meetings with a relevantly-trained individual (for example, brief behavioural activation in depression).
- A set of common factors to form part of the core competences of any psychological intervention.
- A distinction between general and problem-specific CBT competences that are required to deliver effective CBT.

- Treatment manuals used in trials of effective interventions.

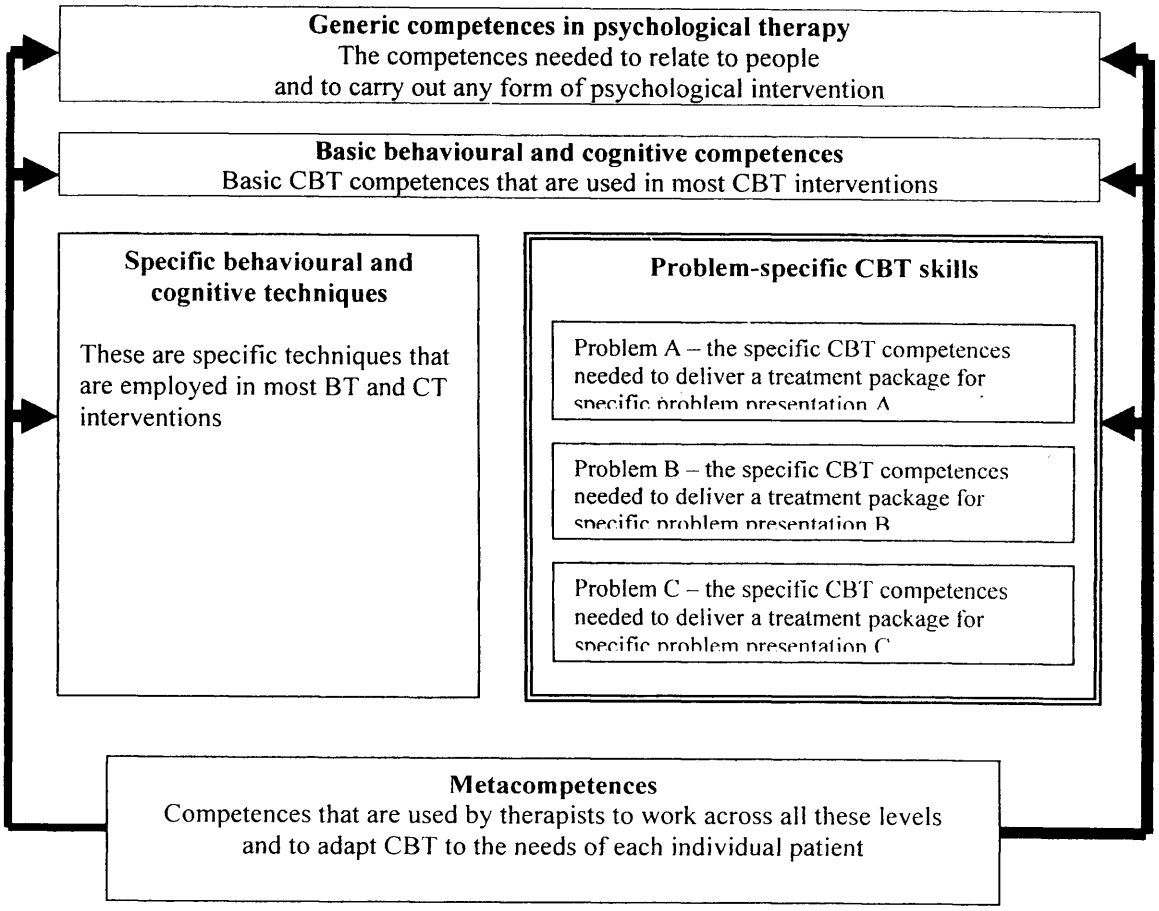
## 5.5 An overall model for CBT competences

Although the focus is on CBT competences, some of the elements are common to all psychological therapies. For example, all individuals providing psychological interventions need to be able to demonstrate basic skills, such as a capacity to relate to clients in a manner that is warm, encouraging and accepting. The basic structure of the model is set out in Figure 5.1 and its essential features are set out below.

### Generic competences

These are the competences that need to be employed in order to carry out any psychological intervention. These refer to key aspects of the therapist–client relationship, without which specific technical interventions are less likely to succeed, and the ability to operate within professional and ethical guidelines.

**Figure 5.1: Outline model for CBT competences**



**Basic behavioural and cognitive therapy competences" and "specific behavioural and cognitive therapy techniques"**

"Basic" competences establish the structure of the intervention, and form the context for the implementation of specific behavioural and cognitive therapy techniques, which are the core technical interventions employed in most CBT applications. They represent fundamental characteristics of the CBT approach, and form the central core of the intervention because they structure it. They may include agenda setting and the use of "homework" tasks. In contrast, "specific behavioural and cognitive therapy techniques" refers to the set of commonly applied techniques found to a lesser or greater extent in most forms of CBT (for example, the use of thought diaries, guided discovery or behavioural experiments).

**Problem-specific competences**

This refers to the set of competences that comprise interventions for specific disorders, as described in treatment manuals. These are the specific procedures for which there is evidence of benefit for particular problem presentations (for example, the use of exposure to the traumatic event in the treatment of post-traumatic stress disorder, or behavioural activation in the treatment of depression). Since many of the competences included in manuals will have already been described under the headers of generic, basic or specific skills, the competences described as "problem-specific" are fairly targeted.

**Metacompetences**

A common observation is that carrying out a skilled task requires the person to be aware of why and when something is and is not done. Reducing psychological therapy to a series of rote operations would make little sense, and the procedures used to guide practice, which operate at all levels of the model, are referred to as metacompetences. Although there is a sense that these are higher-order competences, it is important that these are not seen as the exclusive preserve of high-intensity interventions, since (to a greater or lesser extent) any intervention will require them.

### 5.6 Identifying the competences to deliver low-intensity psychological interventions

The structure set out above, therefore, provides a framework within which to locate the competences required to deliver low-intensity interventions. Almost invariably treatment trials are conducted using a manual which describes the treatment model and techniques used and therefore represent an ideal version of the required therapist competences. It therefore follows that focusing on manuals associated with the delivery of effective treatments should allow for the identification of key therapist behaviours associated with good outcomes. A major advantage of this approach is that it uses the evidence base to significantly determine which competences should or should not be included. However, it should be recognised that manuals are packages of interventions/techniques, some (or all) of which may be mutative, but others may be irrelevant. Because there are few trials which directly contrast alternative or "dismantled" versions of interventions against each other it is usually not possible to determine exactly which parts of an intervention, and which processes, promote change. It is also important not to treat manuals as a set of rigid rules, all of which must be applied in every case. Clearly clinical judgment is required for the appropriate application of a set of interventions, refined over time by research that identifies the mutative elements.

In light of this, the development of the competences was overseen by an expert reference group comprising recognised experts in CBT, including individuals with expertise in the development of novel CBT treatments, the evaluation of CBT in formal trials, and the development and delivery of supervision and training models in CBT. (See Appendix K for the membership of the expert group).

### 5.7 Method

The methods used for the identification of low-intensity psychological interventions for depression followed the general method (Roth & Pilling, 2007a) used to identify competences for all psychological interventions. It comprised three key elements: first, a review of the manuals for each identified intervention in which the key competences for each intervention were extracted from the manual; second, a validation process by relevant experts including the developers of the intervention and/or authors of the

manual; and third a review by an independent expert advisory group selected because of their special knowledge and expertise in the field.

**Identifying the competences for low-intensity interventions**

As previously discussed two interventions were identified when developing low-intensity interventions for depression: brief behavioural activation (Jacobson *et al.*, 1996; Hopko *et al.*, 2003; Leujec *et al.*, 2003) and guided self-help (Burns, 1999; Holdsworth *et al.*, 1996; Leibowitz, 2002). The expert advisory group expressed significant concern about the applicability of many of the commonly used guided self-help manuals in the literature (for example, Burns, 1999), which often provided only limited guidance to professionals and which were also viewed as too long and complex for routine use in primary care settings with individuals who may have limited literacy skills. Therefore, based on the advice of the expert group, manuals developed and evaluated specifically for the primary care services in the UK (Holdsworth *et al.*, 1996; Leibowitz, 2000) were used as the basis on which to develop the set of competences for the delivery of guided self-help.

The relevant manuals were then identified. In the case of brief behavioural activation this was a relatively straightforward procedure: the manual by Leujec and colleagues (2003), which was used in the trial by Hopko and colleagues (2003) was chosen. For guided self-help, the manuals developed by Holdsworth and colleagues (1996) and subsequently modified for use by PCMHWs (Leibowitz, 2002; Leibowitz *et al.*, 2007) were supplemented by a manual on basic psychotherapeutic skills in primary care developed by Professor David Richards (Richards, 2005), based on a number of trials of self-help interventions in primary care (for example, Mead *et al.*, 2005).

The author (SP) reviewed the relevant manuals and extracted an initial list of the competences, which were fitted into the broad structure set out above. These were then reviewed by another senior clinical psychologist against the original manuals; any differences in the identification or structuring of the competences were resolved by discussion. As far as possible a common style for the competences was adopted that would be both compatible with the overall programme of competences and also be understandable and usable in a number of contexts beyond that developed for the collaborative care programme.

**Validating and reviewing the competences**

The draft version of the competences were then sent both to the developers(s) of the manual and the expert advisory group for comment and further refinement. Subsequent modifications to the competence lists were re-checked with peer reviewers, unless the suggested changes were obvious or obviously uncontroversial. This included comment and discussion on where a particular competence might be best placed in the overall structure; for example pragmatic decisions needed to be made when problem-specific interventions described techniques already included in the list of "specific CBT techniques". In general the intention was to reduce duplication of competences; this could be achieved through cross-referral, for example between the "problem specific" to the "specific technique" list, but if this was not easily accomplished, duplication was permitted. In the preliminary planning stages of the project it was anticipated that validating the competence lists might present a major challenge because it was thought that the identification process may result in lists of undifferentiated competences that would require further sorting in order to separate those which were important from those which were marginal or even redundant. A potential solution was to use Q-sorts (Valenta & Wigger, 1997) to generate consensus expert judgment, but in practice it became clear that a) the competence model developed and b) the quality of material emerging from trials and manuals made this unnecessary, and that few forced choices were required that could not be resolved by the discussion with the relevant individuals or the expert advisory group.

As the competences emerged for low-intensity interventions for depression they were integrated into an overall map and placed under the various headers of "generic", "basic" , "specific" or "metacompetences" (Roth & Pilling, 2007a). The development of this map (Appendix L) was based on the repeated appearance of the same activities in different manuals allowing the map to stay close to the evidence base. It was expected that most of the generic and basic CBT competences could be applied in any low- or high-intensity interventions, but only some of the specific CBT techniques would be required for a problem-specific intervention.

## 5.8 Competences for providing low intensity interventions

The competences required to provide low-intensity interventions are set out below under three headings: generic therapeutic competences, competences to provide brief behavioural activation and competences to provide guided self-help.

### Generic therapeutic competences

The generic therapeutic competences which were extracted from all relevant manuals and are set out in Table 5.1. They fall under three broad headings as set out below.

**Table 5.1: Generic therapeutic competences**

*Ability to engage client*

| |
|---|
| An ability to show satisfactory levels of warmth, concern, confidence and genuineness (matched to client need) while maintaining professional boundaries |
| An ability to engender trust |
| An ability to develop rapport |
| An ability to adapt personal style so that it meshes with that of the client |
| An ability to recognise the importance of discussion and expression of client's emotional reactions |
| An ability to adjust the level of in-session activity and structuring of the session to the client's needs |
| An ability to convey an appropriate level of confidence and competence |
| An ability to avoid negative interpersonal behaviours (such as impatience, aloofness, or insincerity) |

*Ability to deal with emotional content of interventions*

| |
|---|
| An ability to facilitate the processing of emotions by the client—to acknowledge and contain emotional levels that are too high (for example, anger, fear, despair) or too low (for example, apathy, low motivation) |
| An ability to deal effectively with emotional issues that interfere with effective change (for example, hostility, anxiety, excessive anger, avoidance of strong affect) |
| An ability to help the client access, differentiate and express his/her emotions in a way that facilitates change |

*Ability to undertake a generic assessment*

| |
|---|
| An ability to obtain a general idea of the nature of the client's problem |
| An ability to elicit information regarding psychological problems, diagnosis, past history, present life situation, attitude about and motivation for therapy |
| An ability to gain an overview of the client's current life situation, specific stressors and social support |
| An ability to assess the client's coping mechanism, stress tolerance, functional level and capacity for introspection and self-objectivity |
| An ability to help the client identify/select target symptoms or problems, and identify which are the most distressing and which the most amenable to intervention |
| An ability to help the client translate vague/ abstract complaints into more concrete and discrete problems |
| An ability to assess and act on indicators of risk (of harm to self or others) |

## Competences to provide brief behavioural activation

The competences required to deliver brief behavioural activation treatment for depression are set out in Table 5.2. They build on the generic competences and inevitably there is some duplication, for example in the section on establishing a positive relationship. In addition it also includes a section on establishing relationships with professionals, information giving, assessment, and uses of outcome and process measures to help the patient gain from the intervention. This is followed by a section on basic CBT competences, which builds on the generic competences; basic CBT competences are common to all CBT interventions and include establishing a service context for the intervention, providing a rationale for the intervention and decision making regarding the appropriateness of the intervention. A further section on information gathering specific to behavioural activation includes: agreeing the aims of the intervention, facilitating client self-monitoring, facilitating client-led interventions and ending the intervention. The next section focuses on problem-specific competences, including assessment specific to a low-intensity behavioural activation programme, information giving specific to behavioural activation, shared decision making specific to behavioural activation and facilitating behavioural activation. There is a final brief section on meta-competencies.

**Table 5.2: Brief behavioural activation**

| **Establishing a positive relationship with the client** |
|---|
| An ability to develop an empathetic, warm and genuine relationship |
| An ability to communicate effectively through appropriate use of empathic statements, reflection, clarification, verbal and non-verbal behaviours |

| **Establishing good relationships with relevant professionals** |
|---|
| An ability to communicate effectively with professionals about the nature of the client's difficulties, the intervention(s) offered and the outcomes |

| **Giving clients information about depression** |
|---|
| An ability to impart accurate information on the nature and course of depression, and to discuss this with the client |

| **Assessing the client's main problems using a semi-structured interview** |
|---|
| An ability to help the client identify key problem area(s) and to identify the impact of emotional distress on work, home, social and private leisure and close personal |

| |
|---|
| relationships |
| An ability to elicit information regarding diagnosis, past history and present life situation |
| An ability to gather information on current and past treatment (including medical, psychological, social and pharmacological interventions) |
| An ability to gain an overview of the client's current life situation, any specific stressors and their level of social support |
| An ability to use agreed protocols to assess risk to self and others and self-neglect (distinguishing between ideation and intent) |
| An ability to gather information on drug and alcohol use |
| An ability to use appropriate information-gathering techniques |
| An ability to use open and closed question styles flexibly and responsively |
| An ability to phrase questions unambiguously |
| An ability to give the client regular summaries during the interview |

**Gathering information-using measures**

| |
|---|
| An ability to administer and interpret formal measures of mental health for example, Patient Health Questionnaire 9 (PHQ-9), the BDI, activity problem and goal schedules), and to use these both initially and to monitor progress |
| An ability to help clients who need support to complete formal measures |
| An ability to support the client in use of formal measures of mental health to determine the pace of the intervention |

## Basic CBT competences

**Establishing a service context for the intervention**

| |
|---|
| An ability to convey that the intervention is client led and collaborative in nature |
| An ability to convey a context for the intervention, through providing the client with a clear explanation of the practitioner's role |
| An ability to help the client understand the nature and the timing of sessions and the schedule of contacts |

**Providing a rationale for behavioural activation**

| |
|---|
| An ability to provide the rationale for behavioural activation to clients in an encouraging and realistic manner |
| An ability to help the client understand that the main focus of behavioural activation is to increase activities and bring a sense of pleasure or accomplishment |
| An ability to give realistic information regarding outcomes from behavioural activation |

**Decision making regarding the appropriateness of the intervention**

| |
|---|
| An ability to reach agreement with the client that the service is suitable for their needs |
| An ability to help the client decide if behavioural activation (and the circumscribed nature of treatment) is appropriate for their current problems |
| An ability to help the client assess whether they are motivated to engage in a |

| |
|---|
| behavioural activation programme (bearing in mind the link between depressive symptoms and low motivation) |
| An ability to negotiate and agree with the client the next steps in contact (that is, organisational and therapeutic arrangements) |
| An ability to identify clients whose problems lie outside the scope of low-intensity behavioural activation and to liaise with a supervisor to consider referral to alternative interventions |

**Gathering information specific to a behavioural activation model**

**Agreeing the aims of the intervention**

| |
|---|
| An ability to construct and to share a concise problem summary with the client (which includes information on environmental and/or intra-personal triggers, physiological, behavioural and cognitive components of the main problem, and the broader impact of the problem on the client's functioning) |
| An ability to check the accuracy of the problem summary with the client and to agree intervention goals |
| An ability to negotiate and agree the specific components of an intervention based on behavioural activation |
| An ability to help the client prioritise key problem area (s) and identify his/her goals for the intervention |

**Facilitating client self-monitoring**

| |
|---|
| An ability to introduce the rationale for self-monitoring and to help the client undertake this using diaries (including behavioural activation, exposure, sleep and thought diaries) |
| An ability to review diary records with the client, and to discuss any issues or implications that arise from these observations |

**Facilitating client-led interventions**

| |
|---|
| An ability to help the client use self-help materials, including written materials and the use of self-monitoring materials |
| An ability to help clients solve any problems they encounter when using written materials and self-monitoring materials |
| An ability to help the client think through the rationale for performing homework and related tasks, and to help identify and solve any anticipated problems in carrying out tasks |

**Ending the intervention**

| |
|---|
| An ability to negotiate an appropriate end to the intervention, including discussion of relapse prevention |

## Problem-specific competencies

**Assessment specific to a low-intensity behavioural activation programme**

| |
|---|
| An ability to gather information relevant to an ABC model (antecedents, behaviours and consequences) |
| An ability to identify disruptions to the client's routine pleasurable and necessary activities |
| An ability to identify environmental cues for behavioural deficits and excesses |
| An ability to help a client identify desired routine, pleasurable and necessary activities for a programme of behavioural activation |
| An ability to help a client set up, structure and review behavioural activation hierarchy lists including the necessary activities for a programme of behavioural activation |

**Information giving specific to behavioural activation**

| |
|---|
| An ability to discuss with the client the essential components of a behavioural activation programme, including the concepts of depressed and healthy behaviours and avoidance |
| An ability to use written material to communicate the rationale and essential components of a behavioural activation programme |
| An ability to help the client to use written tools for a behavioural activation programme, including hierarchies and behavioural activation diaries |
| An ability to assimilate, review and reflect back to the client information collected in their behavioural activation diaries |

**Shared decision making specific to behavioural activation**

| |
|---|
| An ability to support the client in determining the specific components of their behavioural activation programme |
| An ability to support the initiation of a structured behavioural activation programme in a collaborative, client-centred manner |
| An ability to adjust the pace and content of a behavioural activation programme according to a client's progress and wishes |

**Facilitating behavioural activation**

| |
|---|
| An ability to understand the use, by the client, of behavioural activation materials (including written materials) and self-monitoring materials, and an ability to support the client in their use |
| An ability to help the client think through the rationale for performing homework and related tasks, and to identify and solve any problems they anticipate in carrying out tasks |
| An ability to communicate effectively about the delivery, implementation and monitoring of a behavioural activation programme both in face to face contacts and in telephone contacts |
| An ability to help the client identify and use appropriate rewards for achieving their identified goals |
| An ability to help a client problem-solve any areas of the behavioural activation programme where progress is less than expected |

**Meta-competencies**

| |
|---|
| An ability to maintain a clear distinction between acting as a facilitator of behavioural activation and taking on the more extensive role of a therapist |
| An ability to identify when to persist with the intervention and when to re-evaluate its appropriateness with clients who are not making progress or who show low motivation |
| An ability, in the context of indicators of client progress, to maintain fidelity to the intervention model in the face of client complexity |
| An ability to use supervision to identify gaps in knowledge and understanding, and reflect on and to learn from that experience |

### 5.9 Competences to provide guided self-help

The format (see Table 5.3) for guided self-help broadly follows that of behavioural activation, beginning with a set of generic competences required to establish positive relationships with clients and professionals and obtaining appropriate information. The second section focuses on establishing the framework for CBT-based guided self-help, including giving clients specific information relevant to the intervention, assessing their problems, gathering information using formal assessment methods and decision making regarding the appropriateness of the intervention. This is followed by a set of basic CBT competencies including socialising the client to a CBT model, agreeing the aims of the intervention, facilitating client self-monitoring, facilitating client-led interventions and ending the intervention. As above there is a final brief section on meta-competencies.

**Table 5.3: Guided self-help**

**Generic competencies**

**Establishing a positive relationship with the client**

| |
|---|
| An ability to develop an empathetic, warm and genuine relationship |
| An ability to communicate effectively through appropriate use of empathic statements, reflection, clarification, verbal and non-verbal behaviours |

**Establishing good relationships with relevant professionals**

| |
|---|
| An ability to communicate effectively with professionals about the nature of the client's difficulties, the intervention(s) offered and the outcomes |

**Gathering background information**

| |
|---|
| An ability to gain an overview of the client's current life situation, any specific stressors and level of social support |
| An ability to elicit information regarding diagnosis, past history and present life situation |
| An ability to gather information relating to the impact of emotional distress including |

| |
|---|
| work, home, social and private leisure and close personal relationships |

**Establishing the framework for CBT-based guided self-help**

| |
|---|
| An ability to help the client understand that the main purpose of the intervention is to facilitate the use of self-help material(s) |
| An ability to provide the rationale for guided self-help to clients in an encouraging and realistic manner |
| An ability to establish a context for the intervention, through clear explanation of the practitioner's role |
| An ability to ensure that the client understands the nature and the timing of sessions and the schedule of contacts |
| An ability to convey to the client the client-led, collaborative nature of a self-help intervention |

**Giving clients specific information relevant to the intervention**

| |
|---|
| An ability to impart accurate information on the nature, course and frequency of the presenting problem |
| An ability to give the client information about alternative available evidence-based psychological therapies, as set out in the agreed protocol for the delivery of guided self-help |
| An ability to give realistic information regarding outcomes and the prognosis for the client's condition relevant to the self-help interventions |

**Assessing the client's main problems using a semi-structured interview**

| |
|---|
| An ability to use open and closed question styles flexibly and responsively |
| An ability to phrase questions unambiguously |
| An ability to give the client regular summaries during the interview |
| An ability to use agreed protocols to asses risk to self and others and self- neglect (distinguishing between thoughts, actions and plans) and establish preventative factors |
| An ability to gather information on current and past treatment (including relevant medical, psychological, social and pharmacological interventions) |
| An ability to gather information on drug and alcohol use |
| An ability to identify the key problem(s) through appropriate information gathering relating to the impact of emotional distress on work, home, social and private leisure and close personal relationships |

**Gathering information using formal assessment methods**

| |
|---|
| An ability to administer and interpret formal measures of mental health (for example, PHQ-9, CORE-OM, the BDI, problem and goal statements) |
| An ability to support the client in the completion of formal measures of mental health and to support the client in using these to monitor the content and pace of the intervention |

**Decision making regarding the appropriateness of the intervention**

| |
|---|
| An ability to agree on the suitability of the self-help intervention for the client |
| An ability to collaboratively negotiate and agree with the client the next steps in |

| |
|---|
| contact including organisational and therapeutic arrangements |
| An ability, where necessary in conjunction with a supervisor, to identify clients whose problems lie outside the scope of low-intensity interventions and determine when alternative interventions are required |
| An ability to recognise, where necessary in conjunction with a supervisor, when referral to another part of the service is appropriate |

## Basic CBT competencies

### Socialising the client to a CBT model

| |
|---|
| An ability to communicate the essential components of a cognitive, and/or behaviourally-based self-help programme |
| An ability to communicate the options available to a client within a CBT-based self-help programme |

### Agreeing the aims of the intervention

| |
|---|
| An ability to summarise information gathered from the assessment into a concise problem summary that is shared and checked with the client (which includes information on environmental and/or intrapersonal triggers, physiological, behavioural and cognitive components of the main problem and the broader impact of this problem on the client's functioning) |
| An ability to use the problem summary to agree intervention goals with the client |
| An ability to negotiate and agree the specific components of a CBT-based self-help intervention |

### Facilitating client self-monitoring

| |
|---|
| An ability to support self-monitoring through the use of client-completed diaries (including activity schedules, sleep and thought diaries) |
| An ability to review diary records with the client, and to discuss any implications of these observations with the client |

### Facilitating client-led interventions

| |
|---|
| An ability to understand the use of appropriate self-help materials (including written materials) and self-monitoring materials, and support the client in the use of relevant and effective materials |
| An ability to help the client solve problems encountered when using written materials and self-monitoring materials |
| An ability to help the client think through the rationale for performing homework and related tasks, and to identify and solve any anticipated problems in carrying out tasks |
| An ability to communicate effectively about the delivery, implementation and monitoring of self-help interventions both in face-to-face contacts and in telephone contacts |

### Ending the intervention

| |
|---|
| An ability to negotiate an appropriate ending to the intervention, including discussion of relapse prevention |

**Meta-competencies**

| |
|---|
| An ability to maintain a clear distinction between acting as a facilitator of self-help and taking on the more extensive role of a therapist |
| An ability to identify when to persist with the intervention and when to re-evaluate its appropriateness with clients who are not making progress or who show low motivation |
| An ability in the context of indicators of client progress, to maintain fidelity to the intervention model in the face of client complexity |
| An ability to use supervision to identify gaps in knowledge and understanding, and reflect on and to learn from that experience |

### 5.11 Supporting the delivery of competent low-intensity interventions

It has already been noted that identifying competence, providing training, or gaining considerable experience does not guarantee positive outcomes for patients. Much of the literature on which these conclusions were drawn are from studies of formal psychological interventions and not attenuated brief treatments or guided self-help such as may be provided by case managers in collaborative care. Therefore the importance of the alliance for outcomes and how it might be developed is not well understood. Two approaches have been suggested to deal with this issue. First, that the emphasis shifts from a focus on the alliance *per se* to one which, within a broad CBT framework, emphasises the development of a collaborative relationship (Roth & Pilling, 2007b). This approach is consistent with the educational and exploratory model of delivery of CBT. The second approach builds on that of Leujec and colleagues (2003) and Richards (2005) and emphasises the role of the professional or para-professional in these brief interventions as a coach or facilitator rather than as a therapist *per se*. This is compatible with the notion of a collaborative approach to CBT and is more suited to the model of working with these brief interventions. Developing a collaborative relationship with the therapist acting as a coach then becomes a central element in the training of the individual delivering a brief intervention in a collaborative care programme.

Other important factors also need to be considered, including the assessment for suitability for psychological intervention in a stepped care framework. In a low-intensity intervention it is recognised that the person delivering the treatment may not have the requisite skills to complete a complex assessment. This can be addressed in a number of ways: by establishing clear protocols (which clearly specifies the limits of

the intervention in addition to what it may achieve); giving the client choice, where the "coach" advises but does not decide; by developing effective risk assessment protocols; and by having regular and effective supervision (Gilbody *et al.*, 2006a).

The development of the competences for low-intensity interventions set out above provides an important building block in the development of effective psychological interventions in collaborative care. The details of how this will be achieved are the subject of the development of the collaborative care intervention in Chapter 6.

**Limitations of this review**

This review and development of competences for low-intensity psychological interventions has a number of significant limitations. First, and in contrast to standard psychological interventions, the evidence base is more limited. There are relatively few trials of either guided self-help (which are often quite varied in the nature of the intervention) or brief behavioural activation (Roth & Pilling, 2007a) and the associated treatment manuals are also more limited. As a consequence although there was no significant criticism of the competences from either the developers of the manuals or the expert group there is some uncertainty about how fully the requisite competences have been captured. In addition none of the trials reviewed were undertaken in a collaborative care trial so there is again some uncertainty about the application of the competences to a collaborative care intervention. Both guided self-help and brief behavioural activation manuals also provided little or no guidance on the kind of supervision that is necessary for their successful implementation (Roth *et al.*, 2007) despite its obvious importance in collaborative care. Also, in contrast with standard psychological interventions, there is no evidence linking particular competences to outcomes (Roth & Pilling, 2007b) although it may be reasonable to assume that some core CBT competences such as agenda setting may well link to outcome as they do for standard treatment (for example, Hollon *et al.*, 1992).

The development of these set of competences also involved no field testing; they were not validated against examples of established good practice, for example against transcripts of sessions from high-quality trials of the interventions. The acceptability to those involved in routine practice was also not tested in the external review process and it is possible that the competences prove to be less accessible, and therefore less useful,

to practitioners in the field than they are to experts. Finally, the delivery of an effective collaborative care intervention requires considerable knowledge of a range of mental disorders and it could be argued that their knowledge has not been sufficiently emphasised in the competences developed.

# 6. Development of a Collaborative Care Intervention in the NHS

## 6.1 Introduction

To date there have been few attempts to develop a fully fledged collaborative care programme in the UK that matches the programmes developed by Katon and colleagues in the US (for example, Katon *et al.*, 2001; Simon *et al.*, 2000). As was seen in Chapter 2, the establishment of collaborative care models outside the US has had mixed results (for example, Araya *et al.*, 2003 Smit *et al.*, 2006), and the few UK studies that might be seen to approximate to collaborative care (for example Mann *et al.*, 1998) have not reported a significant clinical benefit. The review by Cape and colleagues (2007) suggested that the attached professional approach developed in the UK produced similar, if not better results, but it may be argued that these largely consisted of efficacy trials and which might generally be expected to have better results than the more pragmatic effectiveness trials that characterised many of the studies from the US (Gilbody *et al.*, 2006b).

The two studies reported by Mann and colleagues (1998) are of interest because they attempted to develop the existing role of the practice-based nurse into a central role within primary care of delivering an intervention closely aligned with the collaborative care model developed in the US. Mann and colleagues (1998) suggest that the lack of effect with additional nurse input could have arisen because of the overall good recovery of participants in both arms of the trial. An alternative explanation is that the nurses did not have a mental health background and were under increasing pressure from other changes in the healthcare system to take on a wide range of responsibilities, for example increased demands for health screening or care of long-tem physical conditions such as diabetes (Department of Health, 2001). Other studies outside the collaborative care field have reported similar problems in attempting to engage practice nurses in mental health interventions (Nolan *et al,* 1999; Wilson *et al.*, 2002). This would suggest that the development of a new or separate role is required if collaborative care is to be successfully adopted in the UK.

Before considering the evidence to support the development of collaborative care in the UK it is helpful to briefly review two issues covered in Chapters 1 and 2: first, the basic

principles of collaborative care that were articulated by Von Korff and colleagues (1997) and second, the approach to the transfer of complex interventions between healthcare systems set out by Hawe and colleagues (2004).

Von Korff and colleagues (1997) identified four essential elements of collaborative care for the effective care of chronic illness as follows:

1. The collaborative definition of problems, in which patient-defined difficulties are identified alongside medical problems diagnosed by healthcare professionals.
2. The focus on specific problems where targets, goals and plans are jointly developed between patients and professionals to achieve a set of realistic objectives.
3. The creation of a range of self-management training and support services, in which patients have access to services that teach the necessary skills needed to carry out treatment plans, guide behaviour change, and provide emotional support.
4. The provision of active and sustained follow-up, in which patients are contacted at specified intervals to monitor health status, identify potential complications, and check and reinforce progress in implementing the care plan.

These essential elements have been refined and developed for the treatment of depression in primary care by Katon and colleagues (for example, Katon *et al.*, 2001; Simon, 2006) to focus on the use of evidence-based protocols for treatment, the development of a structured collaboration between primary care providers and mental health specialists, the active monitoring of adherence to treatment (predominantly pharmacological treatment) and of outcomes, and the provision of psychological interventions in primary care. It is interesting to note that in the development of collaborative care for depression there has been less emphasis on the use of self-help strategies despite the evidence for the efficacy of these interventions and the emphasis given to such approaches by the original developers of the model (for example, Wagner *et al.*, 2002).

The problems of transferring complex interventions between different healthcare systems have previously been reviewed in Chapter 1. Indeed some have argued that complex interventions are essentially "non-transferable" (Tones, 2000). However,

others have rejected this approach (Hawe *et al.*, 2004), arguing that it treats a potentially complex intervention as a simple one. Hawe and colleagues (2004) argue that in complex interventions it is the function and processes of the intervention (essentially those set out above by Von Korff *et al.*, 1997 and Wagner *et al.*, 2002) that should be standardised and not necessarily the individual components. Such an approach allows the form of the intervention to be tailored to local circumstances and the emerging evidence base, and potentially contributes to improved effectiveness. This approach is useful in guiding the development of collaborative care models for the UK healthcare system where the structure of primary care mental health services are significantly different from those in the US, as may be the availability of mental health professionals (for example, Lovell & Richards, 2000). This chapter is primarily concerned with the necessary adaptations to collaborative care that these different circumstances require.

### 6.2 The effective components of collaborative care

With regard to the overall effectiveness of collaborative care (see Chapter 2 for a fuller review), a number of meta-analyses have established that it is clinically effective (Bower *et al.*, 2006; Cape *et al.*, 2007; Gilbody *et al.*, 2006b) but the question of its cost effectiveness remains uncertain (Gilbody *et al.*, 2006b; Ofman *et al.*, 2004). Although collaborative care for depression has developed over the past 15 years and the intervention has grown in complexity it can be characterised by a number of key elements, which include the following: the use of evidence-based protocols for treatment (in particular for antidepressant medication); the development of a structured collaboration between primary care providers and mental health specialists; the active monitoring of adherence to treatment (again, predominantly for pharmacological treatment) and of outcomes; and the provision of psychological interventions in primary care. In more recent studies of collaborative care these interventions are provided by healthcare workers often called case managers, whose role is designated to undertake case coordination and deliver a set of specified interventions. Meta-regression (Bower *et al.*, 2006; Gilbody *et al.*, 2006b) has also identified a number of possible factors that are associated with positive outcomes in collaborative care. These include: systematic methods for the recruitment of patients to the trials; the use of case co-coordinators with a mental health background; the provision of regular supervision and support with medication adherence. While regression techniques cannot establish causal links, the

fact that there is a "good fit" between the key elements identified both by the regression studies and the developers of collaborative care supports the view that these elements may well be important in promoting positive outcomes.

### 6.3 Organising the effective components of collaborative care

If the approach outlined by Hawe and colleagues (2004) is adopted it follows that the work on guideline implementation and organisational development covered in Chapter 2 also has important implications for the uptake of collaborative care in the UK. These included the work and commentaries by Grimshaw and colleagues (2004) on guideline implementation, Ferlie and Shortell (2001) on multi-level organisational change, Valdejc (2001) and Wensing and colleagues (2006) on service re-design and more specific commentaries by Von Korff and Goldberg (2001) and Kilbourne and colleagues (2004) on collaborative care. A brief summary of this work suggests that without significant re-organisation of services it is unlikely that it would be possible to successfully implement collaborative care in the UK, a view that echoes that of Whitty and Gilbody (2005) when discussing the implementation of the NICE guideline on depression in the UK healthcare system. Taken together with the approach outlined by Hawe and colleagues (2004), these reviews highlight a number of key areas for the organisational change and development required for the effective implementation of collaborative care in the UK. They include:

- clarity about the aim and functions of the programme
- clear leadership for the programme at multiple levels of the system
- clarity about role changes required
- effective protocols for service delivery
- effective decision support systems
- effective clinical information systems
- effective consultation with all elements of the care system involved in the delivery of collaborative care.

Each of these aspects of the organisational and programme development are now dealt with below.

### 6.4 The aims and functions of the programme

The aims of collaborative care have been clearly identified and can be stated as improving the current sub-optimal care of depression in primary care (Simon *et al.*, 1995; Donoghue & Tylee, 1996; Young *et al.*, 2001). The functions are also clearly set out in the discussion of collaborative care summarised above and in more detail in Chapter 2. They include: the collaborative identification of difficulty and the focus on specific problems; the use of a range of self-management training and support services (in which patients have access to services that teach the necessary skills needed to carry out treatment plans, guide behaviour change, and provide emotional support); and the provision of active and sustained follow-up to check on and reinforce progress in implementing the care plan. The key challenge therefore in developing and implementing a collaborative care intervention lies in being able to properly articulate these aims and engage a range of stakeholders, including clinicians providing services, in considering how involvement in a programme could bring about improvements in the services they provide. While the responsibility for this rests in significant part with the leadership of the programme (see the section below for a fuller discussion of this), all participants in the programme need to be clear about its aims and functions and be able to discuss them with key individuals at all levels of the organisation. Education and information about the potential benefits of collaborative care then becomes the concern of all involved in the programme.

### 6.5 Programme leadership

It is clear from the review of the literature that effective leadership of a collaborative care programme requires leadership at several levels of the organisation in which the programme is to be established. With this in mind a steering group was established which could take on the varied leadership roles within the primary care service in which the intervention was to be evaluated. The steering group included: the lead researcher (SP) who also had a clinical and service development role in local mental health services; a GP from one of the two participating practices (see below) who was also an academic with an interest in mental health; a senior clinical psychologist based in primary care who also had a service development role in the local primary care trust (and who would lead and supervise the work of the PCMHWs); and a senior clinical

psychologist from the local secondary care provider who had been involved in a number of primary mental health developments in local services.

This group also acted as a trial steering committee (see Chapter 7) but took on important leadership roles to support the implementation of the programme. Initial discussions of the group centred on the refinement and development of the details of the model which are described in the sections below. The group had two further important roles: first to integrate the developments in the programme with other planned or already established development in primary care mental health services; and second to communicate these effectively to all relevant elements of the primary and secondary care mental health services.

### 6.6 Role change and development

The review of the literature (for example, Cape *et al.*, 2007; Gilbody *et al.*, 2006b and Bower *et al.*, 2006) identified that the use of staff with a designated case coordination role and a mental health background appear important for the effective implementation of collaborative care. As has already been indicated, one major difference between the UK and US context is the availability of mental health professionals. Simply put, there are not sufficient mental health professionals to provide enhanced input and care coordination for all primary care patients with depression in the UK (Lovell & Richards, 2001). In addition, primary care nurses, who in some programmes have taken on the key role within collaborative care, also have multiple and increasing demands that may preclude a significant role in the care coordination for patients with depression (for example, Nolan *et al.*, 1999). Fortunately a major NHS staffing initiative for primary care mental health had been launched prior to the start of the trial; that is, the development of the new graduate PCMHWs (Department of Health, 2000; Department of Health, 2003). These new workers (characterised by the Department of Health as graduates with a brief general training in mental health) can be seen as the UK equivalents of the graduate mental health workers used in trials of collaborative care in the US by Simon and colleagues (Katzelnick *et al.*, 2000; Simon *et al.*, 2000; Simon *et al.*, 2004). Initial pilot work had already been undertaken with these new workers in local services (Department of Health, 2003; Grayer *et al.*, 2005), which supported the further development of their role in a collaborative care programme. This was integrated

into the local primary care mental health strategy which promoted an enhanced role for PCMHWs in the treatment of mental disorders. The primary focus of the group, then, was on the development of the PCMHW role and the associated process and protocols (the details of these protocols are described below), so that the PCMHWs were able to fully participate in a collaborative care intervention. A crucial element of this was the leadership and organisational development work in the two participating practices, which was led by the clinical psychologist based in primary care and the GP member of the steering group.

### 6.7 Effective protocols for service delivery

In addition to the primary care mental health strategy that assisted the role of the PCMHWs in delivering collaborative care, other development work had already been undertaken that supported the implementation of collaborative care. This was a locally agreed protocol for the treatment of depression (developed by a group led by the senior clinical psychologist from the primary care trust) based on a draft version of the NICE guidelines on depression and anxiety (NICE, 2004a & b) (see Appendix M), which provide evidence-based guidance for the use of pharmacological and psychological interventions for depression and anxiety in primary care.

Further work on the identification of the individual components of the work of the PCMHWs, as set out below, was guided by the evidence summarised in Chapters 2, 3 and 4. The individual elements of the programme are dealt with below in turn.

#### Antidepressant medication

The review in Chapter 3 established that antidepressants (specifically the SSRIs) are effective in the treatment of depression, in particular moderate to severe depression, but that considerable difficulties with the uptake of antidepressants remain and that there are also significant problems with adherence. The first-line use of SSRIs was supported in the local guidance (see Appendix M) and reinforced by an audit programme led by the local pharmacists (Camden PCT, 2004). However, supporting patients in adhering to antidepressants was not part of the local protocol and so became an element of the collaborative care intervention. An information booklet to assist medication adherence was developed; it was based on the work of Katon and colleagues (2002) (which had been used in a number of collaborative care programmes in the US) and the advice

leaflets produced by the UK Psychiatric Pharmacy Group (UKPPG, 2007; www.ukppg.org.uk/ukppg-pals.html).The booklet was developed by the steering group led by the GP and the clinical psychologist based in primary care, and was also sent for external review by an independent expert pharmacist. The booklet had a strong psychoeducational component and also provided information on potential side effects. It was offered to all the patients prescribed antidepressant medication at first contact with the PCMHW and any difficulties and concerns the patient had at the time were discussed. The patient was also able to contact the PCMHW by telephone if they had concerns about medication and the PCMHW also had the option of offering a further telephone call(s) if it was agreed with the patient that this could be helpful. The agreed protocol for the management of problems with medication set out that where difficulties arose the PCMHW, and/or the patient as appropriate, could contact the GP to seek further advice.

**Psychological interventions**

Guided self-help and brief behavioural activation were identified as possible interventions to be delivered as part of the collaborative care intervention (see Chapter 4). The steering group decided to focus primarily on the use of guided self-help in significant part because a well-established training programme for the intervention already existed in the locality. In addition, there was a concern that the PCMHWs may find it too demanding to deliver two distinct interventions in the study. It was also recognised that a significant number of the patients presenting to the programme who met criteria for depression may also be suffering from significant anxiety disorders; the steering group took the view that the guided self-help approach may have slightly more flexibility in meeting the needs of such people than an approach based solely on behavioural activation. However, it was agreed that the focus of the guided self-help intervention for depression should have a strong emphasis on behavioural activation.

In order to facilitate the delivery of guided self-help, three self-help booklets were used that covered depression, stress, and anxiety and panic. In line with the evidence base they were based on CBT principles with a strong psychoeducational component, and in the case of the depression booklet emphasised behavioural activation. They were originally developed by Holdsworth and colleagues (1996) and subsequently modified by Leibowitz (2002) for use by PCMHWs. They were further adapted for the trial and a

revised set published for use in the trial (Camden PCT and UCL, 2004a, 2004b, 2004c and 2004d). The use of guided self-help materials on anxiety was included as there is significant comorbidity (over 50% between anxiety and depression). In developing the booklets a key concern of the steering group was to make them accessible, therefore attention was paid to the language and the length of the booklets. At less than 20 pages, they are considerably shorter than many others used in research studies; the steering group was keen to encourage wide uptake and the absence of any clear evidence of preferred format (Gellaty *et al.*, 2007) supported this position. In discussion with the individual patient, the PCMHW would aim to identify specific goals in the initial assessment and then advise him or her on the use of the appropriate booklet(s) to help achieve the goals.

The protocols for the delivery of the collaborative care intervention stressed the guided self-help element; the full protocols can be seen in Appendix N. They set out an expected range of contacts, with up to three face-to-face contacts and a range of telephone contacts (between one and three). However, PCMHWs were also encouraged to use their discretion in the use of face-to-face contacts and telephone calls; for example, it was possible to offer further telephone contact if there was concern about goal setting or other difficulties with the use of self-help materials or medication.

**The co-ordination of care**

This is an essential element of the collaborative care programme, but as studies both inside and outside the field of depression have demonstrated, it is unlikely to be sufficient in itself to improve care (for example, Goldberg *et al.*, 2004; Kendall *et al.*, 2002). The case coordination elements of the intervention had a number of important aspects, including case finding or identification, coordination of care inside and outside the practice (through the support offered to individuals seeking help with attending specialist clinics), and communication with patients and other professionals. The protocol also contained the outline of a structured mental health assessment and advice on record keeping. (The assessment section also included provision for the assessment of risk and clear advice on the action to be taken if increased risk was identified, for example increased risk of suicide.)

For both participating practices a protocol was developed for the identification of all new cases of depression presenting there; this was common to both practices but was adapted to the needs of each one individually (see Chapter 7 for details of the case finding strategies). A communication and support protocol was also developed between the GPs and the PCMHWs and again further refined for individual practices (Appendix N). Agreed methods for communication included direct contact with professionals, reminder notes, entry into patient medical records and regular attendance at appropriate practice meetings. PCMHWs also supported patients in accessing other services, including specialist mental health or psychosocial intervention programmes. This could include, for example, telephone calls to remind individuals of appointments and, where appropriate, escorting people to appointments. In the initial discussion of the programme with each practice, considerable care was taken to obtain clear agreement from the practice with regard to the case coordination protocols. This process was led by the senior clinical psychologist based in primary care and supported by the GP member of the steering group.

Training was provided in the delivery of all the above protocols by the senior clinical psychologist and the GP member of the steering group assisted by another colleague in primary care who has considerable experience of training para-professional staff in the delivery of guided self-help in primary care settings. The PCMHWs who delivered the interventions where trained in self-help and medication support within a group with other PCMHWs delivering similar intervention outside the trial. Training in the trial-specific protocols, such as the case finding strategies and the communication protocols, was delivered by the senior clinical psychologist from the steering group.

**Decision support systems**

The primary decision support systems were the protocols described above and the regular weekly supervision that the PCMHWs received during the course of the study. This supervision was provided by the senior clinical psychologist based in primary care and was consistent with the approach adopted by Katon and colleagues (2004) and identified by Bower and colleagues (2006) and Gilbody and colleagues (2006b) as being associated with positive outcomes in collaborative care.

**Clinical information systems**

No clinical information systems were developed specifically for the trial; instead adaptations were made to the existing information systems in the two participating practices. These included the use of systems for identifying new cases (see Chapter 7), communication about patients between PCMHWs and other primary care staff, the uptake of antidepressant medication, review of contacts with the services, outcome of any of contacts with specialist secondary care services and the use of community resources.

**Effective consultation**

The study took place in two equal sized inner city general practices located in the same London borough with a combined list size of over 14,000. It began with a 6-month period during which the PCMHWs' role was developed along the lines set out above and modification and developments of the protocol were made in conjunction with the two participating practices. These adjustments were overseen by the steering group, day-to-day discussion of which was led by the clinical psychologist based in primary care, who also had a liaison role with the practices. Participation of the practices was also encouraged by involving them in appointing the PCMHWs.

## 6.8 Limitations in the design of the collaborative care intervention

The intervention described above was developed following a careful review of the evidence on the successful implementation of collaborative care in the US and similar programmes in the UK and Europe. It also drew on reviews of the evidence on the effectiveness of psychological and pharmacological interventions. A consideration of the structure and content of the interventions used in the trial suggests that they meet the broad definition of a collaborative care initiative and also meet the requirement set out by Hawe and colleagues (2004) for an intervention that provides the essential functions while not attempting an exact, and therefore potentially flawed, replication of the precise details of the programme.

However, the intervention has a number of limitations when compared with the collaborative care programmes developed in the US. These include: the lack of provision of study-specific antidepressant treatment protocols; the lack of prior mental health experience of the PCMHWs; a lack of specialist mental health input (for

example, there was no direct provision of expert advice to the practices [as opposed to the PCMHWs] from a consultant psychiatrist or senior psychologist); and the limited clinical information systems (while use of the existing systems may have promoted integration, it was not possible to fully integrate the protocols into the information systems). The intervention also did not include any case finding element, which a number of more recent collaborative care interventions have built into collaborative care (for example, Hunkeler *et al.*, 2006). (Although case finding did occur in the study [see Chapter 7] it should properly be seen as a recruitment strategy for the trial and not a formal part of the intervention itself.)

In addition, although this study sought to give a more prominent position to psychological interventions, limitations in the estimated capacity of the PCMHWs to deliver more complex interventions, and the limitations of resources available to the study, meant that guided self-help was chosen as the primary psychological interventions even though the evidence base for its effectiveness, especially in the longer term, is limited. Constraints imposed by the research design may also have hampered the uptake of certain interventions, for example the requirement to identify and consent patients before initiating medication support meant often that a delay of over 2 weeks may have occured between the prescription of an antidepressant and contact with the PCMHW.

# 7. Trial Design

## 7.1 Developing the evaluation of a collaborative care model for depression

This chapter describes the development and design of an exploratory RCT of collaborative care. Collaborative care is a complex intervention and as such its evaluation requires several stages. A model for the evaluation of complex interventions has been set out by Campbell and colleagues (2000) and by the Medical Research Council (2000); it involves a phased approach as follows:

*Pre-clinical phase* - relevant theory is reviewed to ensure the most effective interventions are chosen, the correct hypotheses are identified, major design issues are understood and any potential confounders are identified.

*Modelling* –the components of the interventions are identified, the mechanisms by which they may operate are understood and the potential interactions between the interventions are also considered.

*Exploratory trial* –the constant and variable components of an intervention are described and a feasible protocol, including comparing the intervention with an appropriate comparator, are developed and tested.

*Definitive RCT* –the fully developed intervention is compared to an appropriate comparator using a theoretically sound and reproducible protocol in a study that has adequate statistical power.

*Long-term implementation* – it is determined whether others can reliably replicate the intervention in the long term in uncontrolled settings.

This thesis is concerned with the first three phases of the development and evaluation of a complex intervention; that is, through to the development of an exploratory trial. The first two elements of the evaluation have been the focus of the preceding six chapters, which have reviewed the underlying theory for collaborative care (the chronic disease model); considered the evidence and hypotheses about its likely efficacy; identified the most effective interventions (pharmacological and psychological interventions); identified the potential interactions between these interventions (for

example, the additive value of combined treatments); and considered major design issues (for example, the importance of comparators and the integration of the intervention into the primary care system) and any potential confounders (for example, the availability, and the skills, of the staff required to deliver collaborative care).

In this chapter the focus is on the third phase of the evaluation, in which the work of the preceding chapters is brought together to inform the development and implementation of an exploratory trial. To expand on the outline for phase three above, the more detailed aims of the trial include:

1. developing and testing an intervention against an appropriate comparator
2. testing the acceptability and relevance of organisational changes to clinicians and patients
3. testing the acceptability of the recruitment, engagement and retention strategies used in the intervention
4. testing the acceptability of randomisation to patients and the service
5. testing the acceptability of the intervention to patients
6. testing the acceptability and relevance of a series of outcome measures
7. informing the power calculations for a large-scale trial.

Crucial to achieving the aims set out above is the use of a range of different methods, in addition to the simple evaluation of the outcome of the trial; these methods are often referred to as "parallel process evaluation" and the key elements of such an approach are summarised by Oakley and colleagues (2006). They draw a helpful distinction between interventions that are inherently faulty (a failure of intervention concept or theory) and those that are badly delivered (an implementation failure). In the case of an exploratory trial, the focus is primarily on the former, whereas in a large-scale definitive RCT the concern would be with the latter (for example, significant site differences arising from differences in therapist performance in a trial of a novel psychological intervention). The focus of the process evaluation in this study therefore is on whether the intervention can be delivered in a way that is consistent with the underlying concepts of collaborative care, in a manner that is acceptable to patients and clinicians and produces outcomes that (if lacking in statistical significance) support the

view that the intervention has potentially sufficient effect to be considered for testing in a large-scale trial.

### 7.2 Trial design [13]

The study was an exploratory individually randomised controlled trial of the collaborative care of depression. It compared the delivery of a collaborative care programme for depression delivered by PCMHWs, in addition to usual care, with usual care alone delivered by the primary care team.

An important issue to consider in the design of any trial is how feasible it is to maintain the "blindness" of investigators, clinicians and participants to allocation to trial arms and subsequently to the intervention(s) received (Hoptof, 2002). Typically in a pharmacological intervention the aim is to achieve a double blinding of the intervention; that is, investigator, clinician and participant are unaware of both the method of allocation and the interventions being received. This is usually achieved by producing tablets that are identical, independent allocation to trial condition and independent and blind assessment of trial participants. This is not without its problems; for example, side effects (for instance, tremor with lithium) may be known by patients, clinicians or researchers and may lead to a "breaking of the blind" (Margraf *et al.*, 1991).

The problem of maintaining blindness is much more challenging in trials of complex interventions where clinicians and patients are almost inevitably aware of the intervention, and it is also often extremely difficult to blind an independent researcher from knowing which intervention had been provided (Hoptof, 2002). However, Schulz and colleagues (1995) provide some reassurance; in an empirical study of sources of bias in RCTs they demonstrated that blinding to initial allocation is the most significant factor in reducing the possibility of bias. Further measures such as block randomisation and the use of an independent statistician have also been shown to reduce bias (Hoptof, 2002). Given the problems with ensuring blindness in this trial, such procedures were adopted and participants were randomised in blocks of six by a statistician who was independent of the trial steering group.

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[13] The trial received ethical approval from Camden and Islington Research Ethics Committe Ref: 03/42.

Other potential problems with clinical trials can arise from baseline differences between the two comparison groups, particularly if the groups are small. These problems can be addressed by a number of strategies, generally referred to as "restricted randomisation", including stratification and minimisation (Schulz & Grimes, 2002a; Hewitt & Torgerson, 2006). Both attempt to avoid the problem that in trials with a low number of participants (as in this exploratory trial) it is possible that there will be an uneven distribution of a key characteristics of the patient group which, although occurring by chance, may have a significant impact on the trial outcome and the subsequent analysis of the results. In a treatment trial in oncology where the treatment effects are likely to be modest, but where a baseline prognostic factor (for example, degree of tumour spread) is a potentially powerful predictor of outcome, a combination of block randomisation and stratification was used (Peto *et al.*, 1995). Stratification is generally the preferred method if restricted randomisation is to be used in small trials (Hewitt & Torgerson, 2006), although it is still a subject of controversy, with some advocating the method of minimisation (Altman & Bland, 2003). It is also generally accepted that no more than two factors should be used when stratifying participants for randomisation (Hewitt & Torgerson, 2006).

Given the potentially important impact of socio-demographic factors on the development and maintenance of depression (see Chapter 2), and the considerable differences in the socio-demographics of the two primary care practices examined in the study, practice was chosen as one factor in this study. The other factor was young men (that is, men under 35 years of age); the main funding body for the trial had a specific interest in the impact of the intervention on young men and it was possible that the relatively low number of young men entered into the trial could be unevenly distributed between the two arms of the trail The adoption of these two factors on which stratification was based further supported the use of block randomisation since it offered some protection from referring staff attempting to guess the allocation outcomes and adjusting their referral patterns as a consequence (Schulz & Grimes, 2002b). The randomisation used was a permuted random block randomisation with stratification of participant factors, using Clinstat software (see Bland, 1996).

**Setting**

The trial was based in the primary care services of an inner city London borough. The precise choice of setting was determined by a number of factors, predominantly locally determined. First, issues concerned with the limitations of the resources of the research team influenced the choice of participating practices, with a bias to larger practices (thereby reducing the workload involved in recruitment and limiting the number of practices that the PCMHWs had to work with). Therefore all practices in the borough with a list size of approximately 6,500 or more, which were not close to the borough boundaries[14] and which did not have a significant student population were initially identified. This resulted in the identification of eight practices in the borough. First, practices that also had a track record of supporting research were preferred. Secondly, practices that had populations reflecting the wider population (in terms of social class and ethnicity) served by the local NHS services were favoured. Two of the practices that met these criteria were approached by the research team and agreed to participate in the study.

At the time of initial recruitment to the study, practice 1 had a list size of 6,400 patients and practice 2 had 8,000; by the end of the study this had fallen to 6,200 for practice 1 but had risen to 8,500 for practice 2. Both were based in the same inner city London borough; practice 2 was located in an affluent part (Index of Multiple Deprivation [IMD] 1.9% [Office of the Deputy Prime Minister, 2004]) and practice 1 was in a very deprived area (IMD 54%). Practice 1 had five partners (including three who worked part-time) and four salaried GPs; practice 2 had five partners. Both practices had "in-house" counsellors who provided psychological treatments (in common with 60 to 70% of general practices in the UK [Mellor-Clark *et al.*, 2001]), and had good links and access to a range of secondary care mental health services provided by the same secondary care organisation. While not a representative sample of NHS practices, they did include a range of problems common to the NHS and also provided a range of services usually found there. The primary care mental health services in the borough had experience of developing roles for PCMHWs, although neither of the two practices had previously had a PCMHW placed in the practice.

[14] Given that a key element of the project was potentially facilitating links with secondary care mental health services, practices that were located near borough boundaries and potentially had links with more than one secondary care service were excluded.

Members of the research team had regular contact with the two practices to discuss the detail of the implementation of the trial. Considerable efforts were made to involve both practices, for example in the appointment of the PCMHWs, the refinement and development of trial materials, the design of the flyers to aid recruitment (see below for further details) and the content of all communication with the trial participants. Regular meetings throughout the trial took place between members of the trial steering group and senior staff from both practices to discuss any problems.

**Participants**

In common with the method adopted in most trials of collaborative care, a pragmatic approach was taken to trial recruitment where the identification and diagnosis of depression was led by the clinicians participating in the study. The primary entry requirement was that the individual had to be aged 16 years or older and have a clinical diagnosis of depression established by their GP, with a BDI-II score greater than 10 (Beck *et al.*, 1996). The age limit of 16 was lower than many similar trials and, again, was influenced by the agreement with the funding body to seek to recruit young men to the study. All GPs in the study had a protocol for the assessment and treatment of depression that included ICD-10 (World Health Organization, 1992) criteria for diagnosis. The BDI-II was used both to balance any errors in diagnosis by the GP and, because it was administered by the research assistant or PCMHW during the initial assessment phase of the study, to exclude those individuals who may already have begun to recover from their depressive episode after initial contact with the GP or who were unlikely to meet criteria for diagnosis if recruited through the flyer (see below). All new presentations of depression (including incidence and prevalence cases) were eligible for inclusion in the trial—this is in line with the strategies for recruitment adopted in a number of previous trials of collaborative care (Bower *et al.*, 2006; Gilbody *et al.*, 2006a). However, participants were excluded if they had:

- been treated for depression (that is, in the 4 months prior to identification as a possible trial participant they had been prescribed antidepressants or referred to specialist mental health services)[15]

[15] This was introduced to prevent a potential underestimation of the potential impact of the intervention.

- a current diagnosis of a psychotic disorder, including schizophrenia or bipolar disorder (the presence of such a disorder may also have significantly affected the course of treatment; separate collaborative care programmes have been developed for bipolar disorder [Simon *et al.*, 2006])
- significant drug or alcohol problems, which in all likelihood would have an impact both on the person's rate of recovery and ability to participate fully in the trial.
- significant cognitive impairment (for example, dementia), which may have limited the person's ability to participate in the trial.

In addition to the above exclusion criteria, GPs could also exclude patients who were recruited by means other than GP referral (see the section on recruitment strategies below) if they did not deem them suitable for inclusion in the trial. The basis for exclusion was a clinical decision by the GP and was based on the GP's view as to whether a patient may have been harmed or put at increased risk in some way or would have been unlikely to benefit from inclusion in the trial. This exclusion criterion was agreed with both practices in initial discussions.

**Recruitment**

*Estimated recruitment rate and duration of the study* - As stated above, all patients aged 16 or over, with a diagnosis of depression (subject to the exclusion criteria described above) were eligible for the study. Given the combined list size for both practices of 14,379 patients, an annual prevalence of depression in the adult population of 6% (based on conservative estimates from the National Depression Campaign [1999] and Kessler and colleagues [2003]) and a detection rate of approximately 30% (Goldberg, 1995), it was estimated that about four patients per week would be identified in the study. Of these it was further estimated that at least 50% would decline to enter the trial, resulting in a total of two participants entering the trial each week. Over a 6-month period this would result in approximately 50 individuals entering the trial. However, there is considerable uncertainty in recruitment of patients into trials (Watson & Torgerson, 2006), particularly in primary care, and therefore a number of additional methods other than identification and referral by GPs were developed to increase recruitment, including searching of electronic medical records and direct contact with high-risk groups (see below for details).

Following discussion in the trial steering group, an initial recruitment period of 6 months was agreed as it was thought that a sample of 50 individuals would be recruited from direct GP referral and that this would be augmented by the additional recruitment strategies (see below), perhaps by up to 50%, giving a total sample for the trial of approximately 75. This number was considered to be sufficient to test the feasibility of the trial protocol.

*Recruitment strategies*

Poor recruitment is a common problem for randomised trials and can be even more difficult in primary care studies especially with a disorder like depression, where low volition and stigma can be major barriers to recruitment (Ross *et al.*, 1999; Watson & Torgerson, 2006). Therefore this study explored a number of ways in which this problem could be addressed. Three different methods of recruitment to the study were adopted as described below:

*Referral from GPs* – as stated above the primary route of referral to the study was via GPs who were encouraged to refer all new presentations of depression to the study. When GPs identified depression in people who also met the criteria set out above, they gave them a trial information sheet (see Appendix O) and sought their consent for the research assistant to contact them and invite them to join the study. The research assistant gave patients another copy of the trial information sheet and obtained written consent.

*Electronic medical record system* - the electronic medical record system of both practices was checked on a weekly basis by the PCMHW or research assistant to identify potential participants who had not been referred to the study by the GP. These included individuals who, according to the electronic records, had been given a diagnosis of depression or prescribed an antidepressant but had not been referred to the trial and the records showed no clear decision not to refer the patients. In addition the records also had to show that patients had not been having any active treatment (antidepressants or specialist mental health services) in the previous 4 months. The identified cases were brought to the attention of the GP by the PCMHW; the GP then considered whether it was possible to include the patients in the trial. If this was appropriate, a letter was sent from the practice inviting the identified patients to take

part in the study and to contact the research assistant if they wished to do so (see Appendix O). Patients were then followed up by the research assistant with a telephone call, invited to a meeting and their consent sought to enter the trial, as for a standard GP referral.

*Targeted groups in receipt of a letter and flyer from the practice* - the final route of recruitment to the study involved directly mailing potential participants with a letter from the practice along with a flyer informing them of the service available. This method was based on that developed by Symons and colleagues (2004), which used a depression flyer (a leaflet designed to inform people about and encourage them to seek treatment for depression) to identify all possible patients with depression in one large group practice. Symons and colleagues (2004) concluded that, although a number of patients with depression were identified, the method was unlikely to be cost effective for routine clinical use. For this study the model was adapted with targeted flyers specifically to promote recruitment to the trial. They informed practice patients of a new service that was being offered at the practice and invited them to contact the practice if they felt they may be depressed and would like to discuss the new service. The letters and accompanying flyer were sent to three groups of people who were potentially at increased risk of depression and/or who were identified as being reluctant to seek help for mental health problems. (A copy of the letter and the flyer [both of which were refined in discussion with each practice] are included in Appendix O.) The three groups were:

- Individuals aged over 16 years who were identified from the electronic records system of the practice as having had at least one previous episode of depression but who were not currently in active treatment. The period of time searched varied dependent on the time for which an individual had been on the practice list but typically did not extend beyond 3 years for most patients as, prior to that, direct patient contact data and diagnoses were not entered onto the electronic records of the practices. Given the high recurrence rate for depression (Goldberg *et al.*, 1998) and the reluctance of many people to seek treatment (Meltzer *et al.*, 2000), such individuals seemed to be an important group to target.
- Young men aged under 35 years; this group was targeted because early onset of depression is associated with a significantly increased vulnerability to relapse

(Giles *et al.*, 1989), because young men are far less likely to ask for help even if they are depressed when consulting a GP (Jenkins *et al.*, 1997), and because of the strong association with suicide in depressed young men (HDA, 2004).[16]

- Individuals aged over 16 years with chronic physical health problems, particularly those with physical disabilities such as diabetes, coronary heart disease or arthritis, which are all associated with increased levels of depression (Cassano & Fava, 2002). Depression is also implicated in the prognosis of these diseases, with increased post-MI mortality being positively associated with the disorder (Lesperance & Frasure-Smith, 2000). All people with a diagnosis of the following chronic physical health problems were identified: diabetes mellitus, ischaemic heart disease, rheumatoid arthritis, chronic rheumatoid heart disease, chronic obstructive pulmonary disease and generalised osteoarthritis.

The practices' electronic records were searched to identify all people in the above groups; individuals were only included in the above lists if they had not been in receipt of treatment in the previous 4 months. Once the lists had been generated from the electronic record systems, they were then checked with the identified patients' GP to see whether, in the GP's opinion, a patient should not be sent a letter. When the agreement of the GP had been obtained, all the patients remaining on the list were contacted.

The method of recruitment for the targeted group was different in that the first contact with the service was via the PCMHW and not the GP. (This was because there was initially uncertainty about the response rate to the flyers and concern that it may have generated a volume of work that GPs may not have been able to respond to.) This necessitated a different protocol for assessment, which included referral to the GP for those who were identified as potentially depressed, whether or not they wished to enter the study.

### 7.3 Interventions

The rationale behind the interventions, the protocols for their delivery and the content of the interventions has been described in detail in Chapter 6 and will not be repeated here.

[16] Suicide remains the most common cause of death in men under 35 (Department of Health, 2002).

The enhanced care programme was delivered by PCMHWs who received a careful introduction into each practice, were trained in carrying out a structured mental health assessment and were also trained to deliver the interventions, according to well-defined protocols. In total three PCMHWs delivered the intervention; two in Practice 1 (one of the PCMHWs left to take up a new post before recruitment to the trial was complete) and one in Practice 2. All three PCMHWs were female psychology graduates in their early to mid twenties with limited experience in mental health care and no previous experience of enhanced care or low intensity psychological interventions of the kind delivered in this study. They were the only staff members delivering these interventions in the practices. The interventions, as described in Chapter 6, included guided self-help, support in taking medication, referral facilitation and co-ordination of care.

The PCMHWs received weekly supervision from a senior clinical psychologist and were able to contact the psychologist or a senior clinical member of the practice on a daily basis if they needed urgent advice about the clinical management of a patient. No limitations were placed on the availability of the range of primary and secondary care mental health services (for example, the use of antidepressants, referral to "in-house" counselling services and/or referral to secondary care services) in either the enhanced care or usual care arm for any of the study participants.

Irrespective of the route by which patients were recruited to the study, all had an initial session with the PCMHW, which lasted approximately 45 minutes and included: a description of the nature of the services available; a structured clinical interview covering current problems and previous history of depression; and information about current and past treatments, along with a risk assessment (see Appendix P for details of this assessment). In the case of the participants recruited by the flyer, a fuller explanation of the study was given and if patients expressed an interest in participating in the study they were referred to their GP for assessment and consent to enter the study. In line with the agreed protocols each participant would normally expect to receive two to eight contacts with the PCMHW over a 4-month period. The first contact with the PCMHW was face to face but subsequent contacts could either be face to face or by telephone. The duration of contact had a maximum time limit of 4 months and during

this time PCMHWs were expected to provide a minimum of one and a maximum of three face-to-face contacts. In addition they could provide up to five telephone contacts.

### 7.4 Outcome measures

All outcome measures at baseline, 4-month and 8-month follow-up were collected where possible in a face-to-face interview with the trial research assistant; where this was not possible or where incomplete follow-up questionnaires were returned, participants were contacted by post and/or by telephone.

Primary outcome measure

The primary outcome measure for the study was the BDI-II score (Beck *et al.*, 1996) at 4 months. Four months was chosen as the time point for the primary outcome measure as it was at the end of the intervention period and would be likely to give some indication of the maximum effect of the intervention and also provide important information on retention rates for the trial. The BDI-II is a 21-question multiple-choice self-report questionnaire with scores ranging from 0 to 63. It is one of the most widely used instruments for measuring the severity of depression and is a development of an earlier version of the questionnaire (Beck *et al.*, 1961), which was revised to bring it in line with DSM-IV. The questionnaire is designed for adults age 17-80 and is composed of items relating to depression symptoms such as hopelessness and irritability, and cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex. It is a widely used and well-validated self-report measure of depression with good psychometric properties. The use of the self-report measure potentially addressed, albeit to a limited extent, the issue of.

**Figure 7.1: Timeline for outcome measurement**

| **Baseline measures** | **4-month follow-up** | **8-month follow-up** |
|---|---|---|
| BDI-II[1] | BDI-II | BDI-II |
| SF-12[2] | SF-12 | SF-12 |
| WSAS [3] | WSAS | WSAS |
| | CSQ-8[4] | |

[1]Beck Depression Inventory [2] Short Form-12 [3] Work and Social Adjustment Scale [4] Client Satisfaction Questionnaire 8.

**the non-blinding of the intervention in that it was patient-completed and not researcher-rated. Figure 7.1 sets out the protocol for the use of all the outcome measures employed in the trial**

**Secondary outcome measures**

In addition to the BDI-II, three other secondary outcome measures were included. These measures were intended to measure other important aspects of the trial outcome including social and personal adjustment, satisfaction and quality of life, all of which address separate but potentially important aspects of the outcomes of the intervention. Their inclusion also addresses a number of criticisms of existing trials that often focus only on symptomatology or the presence/absence of a disorder (Green, 2006; Pilling & Price, 2006).

*Personal and social functioning* – was measured by the Work and Social Adjustment Scale (WSAS; Marks, 1986), a five-item scale covering work, domestic responsibilities, personal relationships, and social and private leisure activities. Each item is rated on an eight-point scale from 0 (no impairment) to 8 (very severe impairment), giving a maximum score of 40. It is a self-report scale with good reliability and validity (Mundt *et al.*, 2002) and has been used in a number of studies of depression (for example, Mundt *et al.*, 2001).

*Quality of Life* – measured by the Short Form-12 (SF-12), a 12-item shortened version of the SF-36 (Ware *et al.*, 1994); both are widely used measures of quality of life across mental health and a broad range of diseases. The SF-12 is a self-report five-level forced-choice questionnaire, which has good reliability and validity and measures both physical and mental health components of quality of life (Ware *et al.*, 1995, 2002). The two components are reported separately. The SF-12 is likely to be most effective for obtaining a general view of the quality of life. It has been widely used in a number of mental health studies including trials of collaborative care (for example, Wells *et al.*, 2000). The SF-12 was chosen over the SF-36 because of concern about the burden of questionnaire completion on the trial participants.

*Satisfaction with the services provided* – was measured by the Client Satisfaction Questionnaire (CSQ-8; Larsen *et al.*, 1979). The CSQ-8 (Nguyen *et al.*, 1983) is an eight-item questionnaire that was developed from a longer version called the CSQ-18

(Larsen *et al.*, 1979). It has been shown to measure service stratification and the ratings obtained are to some degree independent of symptom-focused outcomes (Nguyen *et al.*, 1983). It covers satisfaction with issues such as the amount of help received, the helpfulness of the services, whether the patient received the service(s) he/she wanted and the quality of service received. Each item is scored on a four-point scale, where the responses cover a poor service through to an excellent service. Scoring is by simple summation, with scores in the range of 8-32. A total score is calculated to indicate an overall level of satisfaction categorised as low (8-20), medium (21-26) or high (27-32) (Waxman, 1996). It is widely used (for example, in the evaluation of satisfaction with primary care mental health staff [Gilbert *et al.*, 2003]) and reports suggest good psychometric properties, but it is potentially susceptible to variance in administration effects (Nguyen *et al.*, 1983). The CSQ-8 was measured at 4 months only but the WSAS and the SF-12 were measured at 4 and 8 months.

### 7.5 Process measures

The process measures used in the study can be divided into two broad groups: a series of quantitative measures concerned with the delivery of care and a more limited exploration of the experience of the delivery of the intervention, which included questionnaires/interviews with participants about their experience of the intervention and two focus groups with the staff of the participating practices. Data for both quantitative and qualitative measures were collected by the research assistant at the 4-month follow-up interview with the patients or, if no meeting could be arranged, the questionnaire was sent by post and followed up by telephone. Other data was also extracted from the PCMHWs' case notes and the practices' electronic records. However, it was anticipated that not all participants would have completed the questions on their experience of the interventions offered; if this was the case the research assistant attempted to complete it (and other elements of the questionnaire) by either face-to-face or telephone interview.

#### Quantitative measures

The quantitative measures, which were collected at the 4-month follow-up interview, can be further divided into those measures that used some form of rating scale to collect

data and those that involved the collection of descriptive statistics on the interventions delivered.

The primary formal measure was the Medication Adherence Scale (Morisky *et al.*, 1986). The adherence scale is a commonly used medication adherence questionnaire composed of four yes/no questions about past medication use patterns and is quick and simple to employ. It was integrated into a longer follow-up questionnaire (see Appendix P) for the data collected from both those in the collaborative-care arm and those in the treatment-as-usual arm. Both questionnaires asked for a general rating of well-being, what treatments were offered and taken up (in addition to that provided by the PCMHWs) and, for those in receipt of collaborative care, a series of questions about guided self-help, the contact with the PCMHW, views of future management and experience of the service generally. For the collaborative-care arm this was combined with data collected by the PCMHWs on the nature of their contacts (face to face or telephone), the content of the sessions (including the offer of guided self-help), advice on medication management, and facilitation of referrals

### 7.6 Qualitative measures

**Individual participant experience**

Qualitative data was also collected at 4 months by using the follow-up questionnaire (see Appendix P). A number of semi-structured questions were included in the follow-up questionnaire and were administered to participants in both arms of the trial. The questions, which were developed by the trial steering group, focused on:

- what led the person to seek help for their depression
- what problems they wanted help with
- what elements of the service were helpful
- whether they gained a better understanding of their depression
- how services could be improved
- reasons for not completing or taking up offers of treatment
- any other comments about the service.

**Staff experience**

In addition to the questions on individual participant experience, two focus groups were held with both practices. These groups were conducted by a senior clinical psychologist who was independent of the research team. The questions in the focus group (see Appendix Q) covered the following areas:

- the practice's views of the overall value of collaborative care
- the recruitment strategies adopted in the study
- the interventions offered during the study
- the demands on the practice of participating in a formal evaluation
- the impact of the study on practice workload
- the role and performance of the PCMHW
- the feasibility of collaborative care in routine practice
- any other comments about the service.

## 7.7 Data analysis

**Outcomes data**

The primary and secondary outcomes were analysed on an intention-to-treat basis with SPSS version 11 (SPSS, 2002). To assess the effect of the intervention on the primary and secondary measures, a linear mixed effects model (with maximum likelihood estimation) was used with adjustment for relevant baseline values. Mixed models are more appropriate than traditional methods for accounting for missing data (Molhenberghs *et al.*, 2004; Beunckens *et al.*, 2005). Review Manager version 4.2.8 (Cochrane Collaboration, 2005) was used to estimate the effect size (standardised mean difference).

**Process data**

Quantitative data was analysed using descriptive statistics and where appropriate simple parametric and non-parametric statistics in SPSS version 11 (SPSS, 2002). Qualitative data was analysed using a modified version of the framework approach as outlined by Ritchie and Spencer (1994). This involved two reviewers independently reviewing a set of transcripts and identifying emerging themes (based on both the data included in the transcript and *a priori* themes agreed between the reviewers) before discussing them

and reaching a consensus on an agreed set of themes. These themes then provided a framework within which the data from the qualitative aspect of the study could be analysed.

**Limitations of the trial design**

The design of the study suffers from a number of limitations. A significant criticism is that it attempted to test two new developments simultaneously: the use of PCMHWs in the treatment of depression and the implementation of collaborative care in the NHS, when the case for neither intervention has yet been established. As a consequence, failure to implement the trial properly may arise from a failure of the PCMHW role and not collaborative care itself (the UK literature suggests that the development of the PCMHW role has been very varied in uptake and succes [Harkness *et al.*, 2006]). However, the services in the borough where the trial took place had done considerable work on developing the PCMHW role (Grayer *et al.*, 2005; Leibowitz, 2007). Collaborative care is a significant organisational intervention and, although the trial steering group made considerable efforts to support this aspect of the trial, it could be argued that the formal evaluation of this aspect of the study is limited and may therefore limit the knowledge gained from the trial. In a similar vein, although there was some review of patient experience, it is possible that there was insufficient focus on this aspect of the trial in the follow-up questionnaires to evaluate participant experience properly, particularly the participants' experience of research aspects of the study such as randomisation.

Resource limitations of the study also led to some overlap in roles between the PCMHWs and the research assistants. This occurred for example in the searching of the electronic databases, the collection of some of the socio-demographic data and the initial introduction to the research aspect of the study by the PCMHWs for those recruited to the study by the flyer. This could have had a number of effects on the recruitment, for example in the exclusion of more severely depressed patients.

The use of young men as one of the two factors on which the stratification of the randomisation was based might also be seen as a limitation of the trial. This arose as a consequence of the interest of one its major funders. It could be argued that a potentially more important factor was method of recruitment, particularly recruitment by flyer,

given that there is some suggestion that recruitment methods can have an impact on the outcome of trials. For example, it has been suggested that the increasing placebo effect seen in clinical trials of antidepressants (Walsh *et al.*, 2002) might be a function of different recruitment methods, including the use of public adverts for trial participants. In addition the focus on young men might require a different approach to the delivery of collaborative care than the one adopted in this study. This may impact both on the nature of the interventions and the way in which care was organised and delivered. No collaborative care studies have so far focused on younger people (Gilbody *et al.*, 2006a) but some have focused explicitly on older people (for example, Unutzer *et al.*, 2002).

The trial was also limited in that it recruited from only two practices and this may restrict the generalisability of the findings. Implementation in smaller practices, with perhaps only two or three GPs may present challenges different from those in the large group practices where the study took place.

The use of the BDI-II as the primary outcome measure may also be criticised, as might the absence of a clinician-rated measure of depression. The use of a measure such as the Patient Health Questionnaire 9 (PHQ-9) (Lowe *et al.*, 2004) could be considered as an alternative self-report measure as it relates closely to the DSM-IV diagnosis for depression and has good psychometric properties. A clinician-rated measure of depression such as the HRSD (Hamiton, 1960) or a diagnostic instrument such as the Clinical Interview Schedule–Revised (CIS–R; Lewis *et al*, 1992) might have been a more effective counter to the use of the cut-off of 10 on the BDI-II for entry to the study.

Related to the above point, the reliance on a GP diagnosis of depression is a significant limitation because, although it was guided by advice on an ICD-10 diagnosis of depression, a formal diagnostic interview was not required for the trial and the use of the cut-off on the BDI-II may not have been a sufficiently robust safeguard. The ability of the GP to exclude individuals from the trial who had been identified as possible participants either through Electronic Medical Information Searches (EMIS) searches or the use of leaflets may also have introduced biases into the study that are difficult to quantify in the absence of data on those individuals who were excluded.

Finally the limited data on the process measures may also limit the lessons drawn from the study. For example, there was no measure in the trial of adherence to interventions such a guided self-help by the PCMHWs, for example by use of tape recording of sessions, and no data on the PCMHWs' own experience, although with only two PCMHWs involved in the trial this may have been of limited value.

# 8. Results (1) – Trial Recruitment and Primary and Secondary Outcome Measures

## 8.1 Introduction

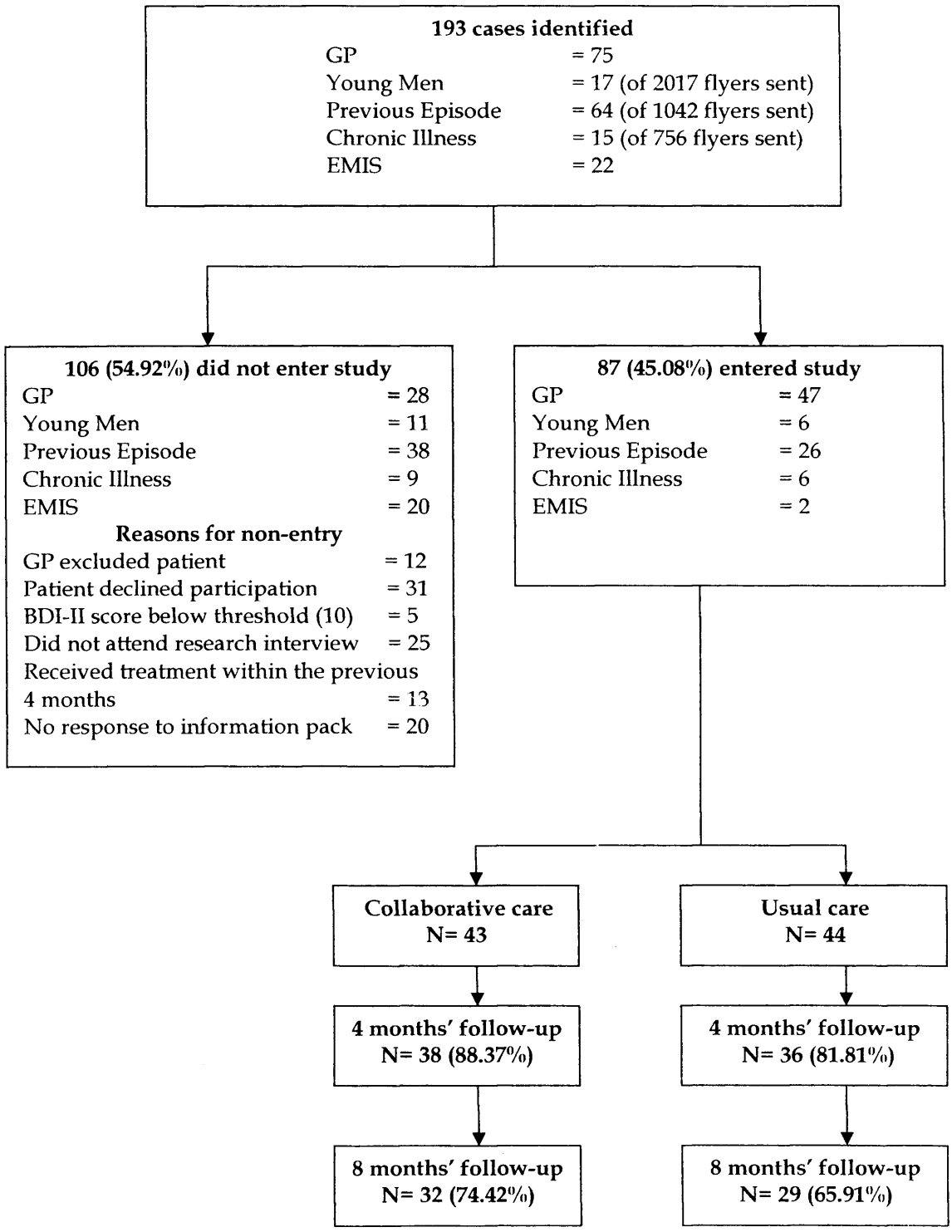
This chapter describes the population recruited to the trial and reports on the analysis of the primary and secondary outcome measures. Chapter 9 will focus on the parallel process evaluation.

## 8.2 Trial recruitment and retention

The data on trial recruitment are set out in a CONSORT (Consolidated Standards for Reporting of Trials) diagram in Figure 8.1. CONSORT is a statement produced by an international group of trial methodologists (Begg *et al.*, 1996) in an attempt to improve the suboptimal reporting of RCTs; this was subsequently revised by Moher and colleagues (2001a). There is evidence to suggest that improvements in trial reporting have followed the production of the original statement (Moher *et al.*, 2001b; Mills *et al.*, 2005). The CONSORT statement is concerned not only with participant recruitment and retention but also several other important aspects of trial reporting, including allocation concealment, randomisation implementation, the blinding status of participants, healthcare providers and outcome assessors, and data analysis, sample size justification, and method of analysis.

The CONSORT diagram describes the process of recruitment for a 9-month period from July 2004 to April 2005. This time period represents an extension of the intended original recruitment period by 3 months and is a function of the initial over-estimation of the recruitment rate to the trial. As can be seen from the diagram, 87 participants were recruited to the trial (44 to the collaborative care arm and 43 to the usual care arm).

**Figure 8.1: CONSORT diagram**




This recruitment rate fitted with expectations and the initial attrition rate of 54.92% (that is of 193 patients identified as potential participants 87 entered the trial) is in line with

other studies in the area. For example, in a sample of collaborative care studies recruitment to a number of trials for which it was possible to obtain broadly comparable data (Araya *et al.*, 2003; Katon *et al.*, 1999; Unutzer *et al.* 2002; Wells *et al.*, 2000 and Miranda *et al.*, 2003) revealed attrition rates of between 38 and 80% with an average of 53%. Follow-up for all participants at 4 months was 82.75% and at 8 months was 68.97% (note, participants were included if data on any primary or secondary outcome measure was obtained). Direct comparison of data is more difficult here largely due to the differing follow-up periods adopted. However, if the above studies are again used as comparators (using the 3-month follow-up data the studies mainly reported) the average follow-up rate was 86% (range 84 to 94%) suggesting that the follow-up rates at 4 months in this trial are broadly comparable with other similar studies.

Of those who did not enter the trial, the largest numbers comprised three groups: those who declined participation when approached by the GP (or in the case of the flyers, the PCMHW) (n= 31 [29.25% of non-participants]); those who did not attend the research interview having previously agreed to consider entering the trial (n= 25 [23.58% of non-participants]); and those who did not respond to the information pack having been identified from the EMIS has having a diagnosis of depression recorded at a recent consultation with the GP (n= 20 [18.86% of non-participants]). These three groups total 76, representing 71.70% of all non-participants. This contrasts with the remaining total of 30 (28.3% of non-participants), comprising those who were excluded by the GP (on clinical grounds that the patient would not likely benefit from or was inappropriate for the trial) (n=12 [11.32% of non-participants]); those who had received treatment within the previous 4 months (n=13 [12.26% of non-participants]); and those who had a BDI-II score below 10 (n=5 [4.72% of non-participants]). These figures suggest that the trial recruitment methods did not result in significant numbers of inappropriate referrals to the trial (for example, the low numbers who scored below 10 on the BDI-II or who were deemed not suitable by the GP) and that the high numbers of those identified by EMIS who did not enter the trial (20 out of 22 [90.90%]) would suggest that the GPs were able to identify likely non-participants in the trial or that the GPs' endorsement of the trial was a significant factor in encouraging participation.

### 8.3 The impact of different recruitment strategies

Three different recruitment strategies were used in the trial. A summary of the outcomes for each of the methods is included in Table 8.1. The first—direct referral from GPs—was responsible for 47 out of a total of 87 participants in the trial (54.02%). The second most significant contributor to trial recruitment was a flyer targeting people with a previous episode of depression but who were not currently in active treatment, which contributed 26 (29.89%) of the trial participants. The other two flyers (targeting young men and individuals with chronic illness) contributed identical totals to the trial, that is six (6.90%) each. As a percentage of the flyers sent, it can be seen that the previous episode group generated a 2.50% return rate, the chronic illness group a 0.79% rate and the young men group a 0.30% rate. An alternative way of expressing these figures would be as ratios, that is 1 in 40, 1 in 127 and 1 in 333 respectively, which, based on an estimate of the cost of each flyer including postage and administration of £1.00, gives an approximate additional cost (based on estimates of time and postage costs) of recruitment to the trial of £40.00, £127.00 and £333.00 respectively for each additional participant recruited. In a trial where, for example, a 100 subjects were recruited by these means, this would increase costs in the region of £4,000 to £33,300; in a large-scale trial costing potentially in excess of £1 million, these modest costs seem worthy of consideration.

Regarding reasons for not participating in the trial, there were few differences or patterns of differences between the various groups that were discernable from the data in Table 8.1. This may be due to the low sample sizes; it is not possible to be certain that with a larger sample size differences may emerge. One difference identified was that the previous episode group recruited via the flyer had a higher percentage of people whom the GP did not deem suitable for the trial (16.07%) when compared with the chronic illness group (8.33%) and the young men (12.50%), but with the small sample size it is not possible to draw any firm conclusions.

**Table 8.1: Summary of the outcomes of different recruitment strategies**

| | Number of potential participants identified | Number entering trial (total n =87) (% of trial participants) | Reason for not entering trial |
|---|---|---|---|
| **GP referral** | 75 | 47 (54.02) | Patient declined =13<br>BDI-II < 10 = 0<br>Did not attend research interview = 11<br>Treatment in past 4 months = 4 |
| **EMIS search** | 22 | 2 (2.29) | No response to information pack =20 |
| **Flyers (total sent)** | | | |
| Previous episode (1042) | 64 | 26 (29.88) | GP excluded patient =9<br>Patient declined =11<br>BDI-II < 10 =2<br>Did not attend research interview =9<br>Treatment in past 4 months =7 |
| Chronic illness (756) | 15 | 6 (6.89) | GP excluded patient =1<br>Patient declined =5<br>BDI-II < 10 = 1<br>Did not attend research interview =2<br>Treatment in past 4 months =0 |
| Young men (2017) | 17 | 6 (6.89) | GP excluded patient =2<br>Patient declined =2<br>BDI-II < 10 =2<br>Did not attend research interview =3<br>Treatment in past 4 months =2 |

## 8.4 Trial participants

### Baseline characteristics

Table 8.2 describes the baseline characteristics of the population included in the trial. As can be seen, there was broadly equal recruitment from both practices (52.9% from practice 1 and 47.1% from practice 2). The average age of participants was 45.92 years with a range of 21 and 87 years. The age range is broadly in line with the sample of collaborative care studies (Araya *et al.*, 2002; Katon *et al.*, 1999; Unutzer *et al.* 2002; Wells *et al.*, 2000 and Miranda *et al.*, 2003) where the age range was between 29 and 71 years; if studies focused on particular age groups such as young women (Miranda *et al.*, 2003) or older adults (Unutzer *et al.*, 2002) are excluded, then the average age range of the studies was between 42.7 and 47.2 years for the interventions groups.

**Table 8.2: Demographic and clinical data at baseline**

| | All participants (n=87) | Collaborative care (n=43) | Usual care (n=44) |
|---|---|---|---|
| **Practice 1 (%)** | 46 (52.87) | 23 (53.49) | 23 (52.27) |
| **Practice 2 (%)** | 41 (47.13) | 20 (46.51) | 21 (47.73) |
| **Age (range)** | 45.92 (21-87) | 44.58 (21-87) | 47.23 (21-80) |
| **Male (%)** | 35 (40.23) | 17 (39.53) | 18 (40.91) |
| **Female (%)** | 52 (59.77) | 26 (60.47) | 26 (59.09) |
| **Ethnic minority (%)** | 24 (27.59) | 12 (27.91) | 12 (27.27) |
| **Married/cohabiting (%)** | 29 (33.33) | 16 (37.21) | 13 (29.55) |
| **Employed (%)** | 39 (44.83) | 21 (48.84) | 18 (40.91) |
| **Previous episode of depression (%)** | 65 (74.71) | 30 (69.77) | 35 (79.55) |
| **Previous treatment with medication (%)** | 32 (36.78) | 18 (41.86) | 14 (31.82) |
| **Other previous treatment (%)** | 27 (31.03) | 17 (39.53) | 10 (22.73) |
| **Baseline BDI (SD)** | 30.82 (11.71) | 30.88 (12.07) | 30.75 (11.47) |
| **Baseline WSAS (SD)** | 27.57 (12.53) | 27.51 (11.88) | 27.63 (13.29) |
| **Baseline SF-12 (SD)** | | | |
| **Mental** | 28.16 (9.04) | 27.95 (9.62) | 28.37 (8.53) |
| **Physical** | 43.92 (13.51) | 44.76 (13.91) | 43.07 (13.21) |

Note. BDI-II = Beck Depression Inventory II; WSAS = Work and Social Adjustment Scale; SF-12 = Short-Form 12; CSQ-8 = Client Satisfaction Questionnaire 8.

Similarly, the percentage of female participants was similar to that in other collaborative care studies (range 66 to 67%), as were previous episodes of depression (range 57 to 76%), but the percentages who were married or cohabitating (33.33%) tended to be lower that that reported in other collaborative care studies (53 to 64%). Comparisons based on other data, such as previous treatment, were not possible as they were either not reported or the data were not comparable with that in other trial reports. The scores on the BDI-II indicate that the average score for the population in the trial was 30.82, that is at the bottom end of the severe range on the BDI-II (Beck *et al.*, 1996), which is somewhat higher than the average for similar trials in collaborative care and for other treatment studies of depression. Scores at baseline on the Work and Social Adjustment Scale (WSAS) as classified by Mundt and colleagues (2002) were in the severe range of impairment. On the mental component of SF-12, the average score fell

within the severe disability range and on the physical component within the mild disability range (Andrews, 2003). The overall picture from the baseline characteristics is of a population with moderate to severe recurrent depression with significant deficits in social functioning and quality of life and with associated disadvantages such as high unemployment and a low rate of marriage or cohabitation. These characteristics suggest that the trial population would not be one where a high spontaneous remission rate would be expected.

An examination of the baseline characteristics of the two populations in the collaborative care and usual care arms does not suggest any major variation in baseline characteristics between populations, indicating that the randomisation had been successful. On two characteristics, previous treatment with antidepressants and any other previous treatment for depression, the difference exceeded 10% and on two others, previous episodes of depression and married/cohabitating, the difference approached but did not exceed 10%.

**8.5 Attrition rates**

Table 8.3 summarises data that compares those who were lost to follow-up (that is, no primary or secondary outcome measure was obtained from the participant) with those who were retained in the trial. It presents the overall loss to follow-up at 4 months and 8 months and then considers a numbers of factors that *a priori* may be associated with this loss, including: gender (because previous trials had suggested a tendency for women to be retained in treatment); employment (as a proxy indicator of social disadvantage); previous episodes of depression (as a measure of chronicity); and BDI-II score (as a measure of severity). The possible association of these factors with loss to follow-up was investigated using regression techniques and the results are also presented in Table 8.3. Of the variables examined, only gender was significantly associated with drop out from the trial at 4 months (B= -2.528, p= 0.02) but this association was not maintained at 8 months (B= 0.916, p= 0.07). An examination of the data shows that the association of gender appears to be a function of a significantly higher attrition rate for women, with 12 being lost to follow-up (23.18% of females in the trial), and only one man (2.86% of males in the trial).

**Table 8.3: Participants lost to follow-up at 4 months**

| | All participants (n=87) | | Collaborative care (n=43) | | Usual care (n=44) | | p value |
|---|---|---|---|---|---|---|---|
| | **Retained in trial** | **Lost to follow-up** | **Retained in trial** | **Lost to follow-up** | **Retained in trial** | **Lost to follow-up** | |
| **Total (%)** | 74 (85.06%) | 13 (14.94%) | 38 (88.37%) | 5 (11.63%) | 36 (81.81%) | 8 (18.19%) | _ |
| **Age** (range) | 47.09 (21-87) | 39.23 (21-66) | 46.50 (21-87) | 30.00 (22-39) | 47.72 (22-82) | 45.00 (21-66) | _ |
| **Male (% of all males)** | 34 (97.14%) | 1 (2.86%) | 17 (39.53%) | 0 | 17 (34.64%) | 1 (2.27%) | p = 0.02[a] |
| **Female (% of all females)** | 40 (76.92%) | 12 (23.18%) | 21 (48.43%) | 5 (11.36%) | 19 (38.63%) | 7 (15.91%) | - |
| **Employed (% of all employed)** | 31 (79.49%) | 8 (20.51%) | 17 (39.53%) | 4 (9.30%) | 14 (31.82%) | 4 (9.09%) | p = 0.63 [a] |
| **Previous episode(s) of depression (% of all with previous episodes)** | 55 (84.62%) | 10 (15.38%) | 28 (65.12%) | 2 (4.65%) | 27 (61.36%) | 8 (19.18%) | p = 0.93 [a] |
| **Baseline BDI (SD)** | 30.89 (12.17) | 30.38 (8.91) | 30.45 (12.38) | 34.20 (9.81) | 31.36 (12.11) | 28.00 (8.02) | p = 0.64 [b] |

[a] Binary logistic regression [b] Linear regression

An examination of baseline depression scores shows the average BDI-II score to be 32.75 (SD 11.69) for women and 27.07 (SD 11.290) for men, a difference of 5.68 but which was not significant ($t = 1.90$, $p = 0.06$). The differential response to treatment by gender has been the source of considerable speculation in the literature on depression. The focus on response to treatment has been almost solely on the response to antidepressants (for

example, Kornstein *et al.*, 2000; Quitkin *et al.*, 2002; Wohlfarth *et al.*, 2004). A comprehensive review of this area is beyond the scope of this thesis, however Goldberg and colleagues (2004) provide a useful summary that indicates that women may respond better to SSRIs than to TCAs, whereas there is some indication that men may respond better to TCAs. The relative impact on drop out from treatment is little researched but there may be an interaction between gender response to and retention in treatment. The data on gender response to psychological interventions is extremely limited with few trials reporting differences in response by gender and as a consequence systematic reviews or meta-analyses do not report much on this issue. Some individual trial data may suggest differences in response, such as the report by Bockting and colleagues (2005) on the poorer response of women to a programme of preventative CBT; they suggest that the result arises because of women experiencing a higher level of adverse events. Similarly a meta-analysis by Jane-Llopis and colleagues (2003) of brief preventative interventions for depression also suggests that men may respond better than women, but the limitations of the data sets used limit the strength of their conclusions. In the area of collaborative care, a number of programmes for women have been developed (for example, Miranda *et al.*, 2003) and have reported outcomes that were generally in line with those for other general adult populations for collaborative care interventions.

### 8.6 Outcome measures at 4 months

Table 8.4 summarises the scores on the primary outcome (BDI-II) and the secondary outcomes (WSAS, SF-12 and CSQ-8) at 4 months. The changes in scores were all in the expected direction; that is, there was greater improvement in the collaborative care condition with the exception of the physical component score of the SF-12, which showed a small improvement in the usual care condition over that in the collaborative care condition. Given that this component of the SF-12 is concerned with physical functioning, it is perhaps not surprising that no change in the expected direction was obtained. At 4 months the average BDI-II score of the collaborative care group was in the mild depression range (Beck *et al.*, 1996) and for the usual care group within the moderate depression range. Average scores on the WSAS were in the moderate range for collaborative care group and severe range for the usual care group. On the SF-12 average mental component score, the collaborative care group was almost in the mild disability range (cut off score 40) while the usual care group were in at the mid point of the

moderate disability range. These data suggest an overall improvement in both groups but one which is more marked in the collaborative care group.

**Table 8.4: Outcome measures at 4 months**

| | Collaborative care | Usual care | Difference between means |
|---|---|---|---|
| **BDI-II (SD)** | 18.64 (12.40) (n=36) | 23.81 (15.19) (n=36) | 5.17 |
| **WSAS (SD)** | 19.34 (13.62) (n=35) | 23.53 (13.18) (n=34) | 4.19 |
| **SF-12 (SD)** | | | |
| **Mental** | 39.04 (10.83) (n=35) | 35.25 (10.92) (n=35) | 3.79 |
| **Physical** | 41.61 (10.21) (n=35) | 43.60 (12.73) (n=35) | 1.99 |
| **CSQ-8 (SD)** | 24.68 (5.50) (n=37) | 21.73 (7.13) (n=33) | 2.95 |

Note. BDI-II = Beck Depression Inventory II; WSAS = Work and Social Adjustment Scale; SF-12 = Short-Form 12; CSQ-8 = Client Satisfaction Questionnaire 8.

As can be seen from the standard deviations around the BDI-II scores there is a considerable range of scores and it is should be noted that only 16 (37.2%) in the collaborative care group and 13 (29.5%) in the usual care group had a BDI-II score below 14[17] (that is no longer meeting criteria for caseness on the BDI-II, Beck *et al.*, 1996). The analysis of the primary outcome (BDI-II score at 4 months) of the trial is set out in Table 8.5.

Before statistical analysis of the data it was examined for normality and the skewness and kurtosis in the data reviewed using SPSS v.11. This showed the skewness and kurtosis to be within acceptable limits. To assess the effect of the intervention on continuous outcomes, a linear mixed effects model (with restricted maximum likelihood estimation and Type III sum of squares) was used, adjusting both for baseline values of the relevant outcome and for employment as fixed effects. The covariates were selected after an initial analysis demonstrated an association with the primary outcomes. Mixed models are more appropriate than traditional methods, such as data imputation, for accounting for missing data (Molhenberghs *et al.*, 2004; Beunckens *et al.*, 2005).

[17] Percentages were calculated based on the assumption that those participants with missing data would have had a BDI-II score of 14 or greater.

(Analyses were done in SPSS v. 11 and Review Manager v. 4.2.8 was used to estimate the effect size [standardised mean difference]).

**Table 8.5: Data analysis at 4 months**

| | Collaborative care | | Usual care | | | | |
|---|---|---|---|---|---|---|---|
| **Outcome measure** | **n** | **Mean (SD)[a]** | **n** | **Mean (SD)** | **Mean difference (95% CI)[a]** | **SMD (95% CI)** | **P value** |
| **BDI-II [b]** | | | | | | | |
| 4 months | 36 | 16.41 (13.62) | 36 | 23.15 (12.16) | -6.74 (-12.82 to -0.66) | -0.52 (-0.99 to -0.05) | .03 |
| **WSAS [b]** | | | | | | | |
| 4 months | 35 | 20.38 (10.14) | 34 | 22.77 (10.93) | -2.39 (-7.47 to 2.69) | -0.22 (-0.70 to 0.25) | .35 |
| **SF-12 - Mental [b]** | | | | | | | |
| 4 months | 35 | 39.76 (10.92) | 35 | 35.13 (10.12) | 4.63 (-0.30 to 9.56) | -0.43 (-0.91 to 0.04) | .07 |
| **SF-12 – Physical [b]** | | | | | | | |
| 4 months | 35 | 41.13 (7.25) | 35 | 44.38 (7.25) | -3.25 (-6.65 to 0.15) | 0.44 (-0.03 to 0.92) | .07 |
| **CSQ-8 [b]** | | | | | | | |
| 4 months | 37 | 24.67 (5.52) | 33 | 21.76 (5.51) | 2.91 (0.32 to -5.50) | -0.52 (-1.00 to -0.04) | .03 |

[a] Estimated marginal means; [b] Covariates – baseline score and employment.
Note. BDI-II = Beck Depression Inventory II; WSAS = Work and Social Adjustment Scale; SF-12 = Short-Form 12; CSQ-8 = Client Satisfaction Questionnaire 8.

As can be seen from Table 8.5, the primary outcome shows a moderate and statistically significant effect. The effect size is towards the upper end of the effect sizes reported in the the meta-analyses of Gilbody and colleagues (2006a), Bower and colleagues (2006) and Cape and colleagues (2007), although it should be noted that most of the effect sizes that they reported were taken around 6 months after initiation of the intervention. The results suggest that it may be possible to replicate the effects of a collaborative care intervention in the NHS and obtain broadly similar results. The data in Table 8.5 also show improved satisfaction in the collaborative care arm of the trial and this is in line with other studies of collaborative care (for example, Badamgarav *et al.*, 2003). On all other secondary outcome measures there were no differences that were either clinically or statistically significant. There was a trend to significance on the SF-12 mental component, which is perhaps not surprising, but no trend on the physical component of the SF-12. More surprising is the lack of any effect on the WSAS given that this has

been shown to be a sensitive measure of change in other clinical trials in mental health (Mundt *et al.*, 2002).

Taken together these data suggest that the collaborative care programme as implemented in this trial can have a positive impact on depression that is sustained until at least 4 months' follow-up in a population with relatively severe depression scores. Further support for the potential imact of the intervention comes from an analysis of those particpants who no longer met criteria for depression (rated as scoring <14 on the BDI-II) using the predicted BDI-II values from linear mixed model (with baseline BDI-II and employment status as covariates). In this analyis there is a moderate but not statistically relative risk favouring the enhanced care group (RR = 1.64 [95% CI 0.84, 3.20] p = 0.15)

### 8.7 Outcome measures at 8 months

Table 8.6 summarises the primary and secondary outcome measures at 8 months. As can be seen from the table there has been a general overall reduction in the differences between the two arms of the trial, which is largely accounted for by a continued improvement in the scores of the usual care group but in the case of the BDI-II scores a small deterioration (1.52). Therefore although the improvement seen at 4 months has been largely maintained, the trial population continue to experience significant problems.

**Table 8.6: Outcome measures at 8 months**

| | Collaborative care | Usual care | Difference between means |
|---|---|---|---|
| **BDI-II (SD)** | 19.88 (13.50) (n=32) | 21.24 (12.04) (n=29) | 1.36 |
| **WSAS (SD)** | 19.72 (14.79) (n=32) | 21.89 (11.23) (n=28) | 2.17 |
| **SF-12 (SD)** | | | |
| **Mental** | 37.50 (12.08) (n=32) | 35.79 (9.06) (n=29) | 1.71 |
| **Physical** | 40.46 (13.36) (n=32) | 41.96 (11.61) (n=29) | 1.50 |

Note. BDI-II = Beck Depression Inventory II; WSAS = Work and Social Adjustment Scale; SF-12 = Short-Form 12.

As can be seen from the analysis of the data (again using a linear mixed effects model) in Table 8.7 the effect size for depressive symptoms at 8 months is still of moderate size but no longer statistically significant. However, the effect size remains at the upper end of the effect sizes reported in the meta-anaylses of Gilbody and colleagues (2006a), Bower and colleagues (2006) and Cape and colleagues (2007) and the follow-up period of 4 months is more in line with the 6-month follow-up period that was commonly reported in those meta-analyses. The lack of a significant result reflects the wide confidence intervals and lack of power associated with the smaller numbers in this analysis. The results further support the suggestion that it may be possible to replicate the effects of a collaborative care intervention in the NHS and obtain broadly similar results.

**Table 8.7: Data analysis at 8 months**

| | Collaborative care | | Usual care | | | | |
|---|---|---|---|---|---|---|---|
| **Outcome measure** | **n** | **Mean (SD)** [a] | **n** | **Mean (SD)** [a] | **Mean difference (95% CI)** | **SMD (95% CI)** | **P value** |
| **BDI-II** [b] | | | | | | | |
| 8 months | 32 | 16.94 (12.90) | 29 | 21.97 (11.34) | -5.03 (-11.25 to 1.20) | -0.41 (-0.92 to 0.10) | .12 |
| **WSAS** [b] | | | | | | | |
| 8 months | 32 | 20.25 (10.66) | 28 | 22.49 (10.82) | -2.25 (-7.83 to 3.33) | -0.21 (-0.71 to 0.30) | .43 |
| **SF-12 – Mental** [b] | | | | | | | |
| 8 months | 32 | 37.25 (10.58) | 29 | 35.40 (10.62) | 1.85 (-3.48 to 7.18) | -0.17 (-0.68 to 0.33) | .50 |
| **SF-12 – Physical** [b] | | | | | | | |
| 8 months | 32 | 40.65 (12.22) | 29 | 41.18 (12.26) | -0.53 (-6.68 to 5.62) | 0.04 (-0.46 to 0.55) | .87 |

[a] Estimated marginal means; [b] covariates – baseline score and employment.
Note. BDI-II = Beck Depression Inventory II; WSAS = Work and Social Adjustment Scale; SF-12 = Short-Form 12.

Given the lack of any significant findings on the secondary outcomes measures at 4 months the absence of differences at 8 months is not surprising on any of the secondary measures.

The data for 4 and 8 months have been presented separately as the primary outcome measure was the score on the BDI-II at 4 months. However, in order to obtain the full benefit of the linear mixed method (that is, to compensate more fully for any missing data) it is advisable to use all data points. In the case of this trial, this involves including the data from 4 and 8 months in the model assuming a first-order autoregressive covariance structure with homogenous variances[18]. When this is done the effect size is in line with the 4 and 8-month data when analysed individually (SMD = -0.46 [95% CI -0.93, 0.00] p = 0.05), is significant and towards the upper end of the effect sizes reported in the collaborative care literature (for example, Gilbody *et al.*, 2006b; Bower *et al.*, 2006).

**8.8 Impact of severity of depression**

In reviewing the components of the collaborative care intervention used in this trial, evidence suggested that the impact on these interventions differed according to the severity of depression. For example, brief interventions such as the guided self-help used in this trial seemed more likely to be of benefit for milder depression and combined antidepressants and CBT more effective for severe depression. The question then arises as to whether or not the effect of the intervention provided in this trial differed according to the severity of depression. Table 8.8 present the outcomes for those participants with moderate and severe depression. A cut off point of 20 or more on the BDI-II (this is indicative of moderate depression in the BDI-II manual [Beck *et al.*, 1996]) was used and the outcomes analysed only for those patients with a score of 20 or more. As can be seen from Table 8.8 the effect size on the BDI-II at 4 and 8 months for the patients with moderate to severe depression is similar to that of the whole trial population suggesting that the intervention can also have a significant benefit for moderate and severe depression.

The pattern of results on the secondary outcome measures for the moderate to severe sub-group is broadly similar to that for the whole trial population. There is significantly greater satisfaction in the collaborative care arm of the trial. Apart from the mental

[18] The robustness of this assumption was tested by re-running the analysis using different covariance structures and then comparing the information criterion.

component score of the SF-12 at 4 months, no other outcomes are significant for this sub-group analysis.

**Table 8.8: Outcomes and data analysis at 4 and 8 months for moderate and severe depression**

| | Collaborative care | | Usual care | | | | |
|---|---|---|---|---|---|---|---|
| **Outcome measure** | **n** | **Mean (SD) [a]** | **n** | **Mean (SD) [a]** | **Mean difference (95% CI)** | **SMD (95% CI)** | **P value** |
| **BDI-II [b]** | | | | | | | |
| 4 months | 27 | 20.26 (13.15) | 29 | 26.98 (12.75) | -6.72 (-13.11 to -0.33) | -0.51 (-1.05 to 0.02) | .06 |
| 8 months | 23 | 22.03 (13.03) | 22 | 25.30 (12.42) | -3.27 (-10.19 to 3.65) | -0.25 (-0.84 to 0.33) | .35 |
| **WSAS [b]** | | | | | | | |
| 4 months | 26 | 23.40 (11.74) | 27 | 25.89 (11.54) | -2.49 (-8.93 to 3.95) | -0.21 (-0.75 to 0.33) | .44 |
| 8 months | 23 | 21.00 (12.51) | 21 | 26.28 (11.41) | -5.28 (-12.60 to 2.03) | -0.43 (-1.03 to 0.17) | .16 |
| **SF-12 – Mental [b]** | | | | | | | |
| 4 months | 26 | 38.64 (10.08) | 28 | 32.41 (9.93) | 6.23 (0.89 to 11.57) | -0.61 (-1.16 to -0.07) | .03 |
| 8 months | 23 | 36.53 (10.38) | 22 | 34.06 (11.12) | 2.47 (-3.82 to 8.76) | -0.23 (-0.81 to 0.36) | .45 |
| **SF-12 – Physical [b]** | | | | | | | |
| 4 months | 26 | 42.06 (11.3) | 28 | 42.01 (11.66) | 0.05 (-6.22 to 6.32) | 0.00 (-0.54 to 0.53) | .99 |
| 8 months | 23 | 40.45 (10.92) | 22 | 41.39 (11.71) | -0.94 (-7.56 to 5.68) | 0.08 (-0.50 to 0.67) | .78 |
| **CSQ-8 [b]** | | | | | | | |
| 4 months | 29 | 24.14 (5.65) | 26 | 20.15 (5.65) | -3.99 (-6.98 to -1.00) | -0.70 (-1.24 to -0.15) | .01 |

[a] Estimated marginal means; [b] Covariates – baseline score and employment.
Note. BDI-II = Beck Depression Inventory II; WSAS = Work and Social Adjustment Scale; SF-12 = Short-Form 12; CSQ-8 = Client Satisfaction Questionnaire 8.

## 8.9 Summary

The analysis of the primary outcome measure suggests that the results reported in collaborative care trials from the US may be replicated in the UK as the effect size

obtained in this trial exceeds the average reported in meta-analyses of that data set (for example, Gilbody *et al.*, 2006b: effect size = 0.25). The effect size in this trial is closer to that obtained for the enhanced professional role (Cape *et al.*, 2007) and it may be that the routine use of a psychological intervention (in this case guided self-help) had some impact on the effectiveness of the overall intervention. The effect size reported in this trial raises the possibility that collaborative care may be cost effective in a UK setting. It is also interesting to note that the effect size for the overall trial population was maintained when the outcome on the BDI-II was analysed for a sub group with moderate to severe depression. (It should also be noted that the overall trial population was rated in the severe category for depression, social functioning and quality of life.) This suggests that the intervention may have value for moderate to severe depression, which is where the major burden of depression lies. However, with the exception of the CSQ-8, no other secondary measure showed a consistent significant effect. This could be due to the lack of impact of the trial intervention on the dimensions covered by the measures, but it may also be due to the limitations of the measures themselves (they may not be sensitive to change in this population) or the trial lacking power to identify significant differences between the two arms. An examination of the data in Table 8.4, Table 8.5, Table 8.6 s and Table 8.6 s uggests that this lack of power might be a possibility with the SF-12 mental component measure but not for the SF-12 physical component measure.

The trial had a recruitment rate that was comparable to other studies in the area and also had similar retention rates throughout the course of treatment. These would further suggest that it might be possible to replicate the trial in the UK. Of the enhanced recruitment strategies employed, the use of leaflets to contact people who had previously been depressed appeared to be the most effective method. For little additional cost, it may be possible to boost recruitment to similar studies. However, it should be noted that the original time for recruitment had to be extended as the number of potential recruits to the trial were below that estimated from the available epidemiological data. Although the lack of a formal independent diagnostic assessment was identified in Chapter 7 as a limitation of the trial, the average baseline BDI-II score, and the small numbers who were excluded on the basis of low BDI-II scores, suggest that the GPs were able to identify patients with major depressive disorder. The attrition

rates from the trial are of some concern, not because they are high but because of the differentially high attrition rate by women, particularly at 4 months. This may have implications for the future design and recruitment strategies for similar trials. However, it should be noted that the numbers in the trial were small (the difference may therefore have arisen by chance) and it was not possible to identify from a review of the relevant literature similar gender-based differences in attrition rates.

### 8.10 Limitations

A major concern with the trial outcomes is the lack of blinding of the assessors to the interventions received by participants; while this is very difficult to avoid in trials of complex interventions it could nevertheless affect the outcome of the trial. The use of different recruitment strategies may alter the composition of the trial participants and thereby limit the comparability with other studies, although screening strategies have been used in a number of collaborative care studies (for example, Unutzer *et al*, 2002). While the attrition rates were not high by the standards of comparable studies, they suggest the need for some caution when interpreting the results because the reasons for participants dropping out of the trial are not well described. The reliance on a self-rating of depression and the absence of a formal diagnostic rating have already been mentioned, but the absence of a formal rating both at baseline and subsequent follow-up is also a significant limitation of the trial. The small numbers in the trial also suggest caution in interpreting differences that emerge in the analysis, for example the gender differences in the trial attrition rates. Lack of information on the reasons for withdrawal from the trial by GPs is also a significant limitation of the trial. Key information for the trial – for example, contacts with GPs and the identification of previous depression – relied on the electronic records, which is a further limitation of the trial. Delays in in offering the intervention to particpants arising from the recruitment and randomisation procedures may also have impacted on the ability of PCMWs to properly deliver the interventions to support adherence to antidepressant medication.

# 9. Results (2) – Parallel Process Evaluation

## 9.1 Introduction

This chapter presents the results of the parallel process evaluation of the clinical trial. It describes and reviews the main elements of the intervention delivered to participants in both arms of the trial. Additional information is provided on the collaborative care intervention and reviewed to ascertain whether the provision of the intervention was in line with the agreed protocols. It also reports on a qualitative exploration of both participant and clinical staff experience of the trial.

## 9.2 The provision of care in the trial

Table 9.1 sets out the key aspects of the provision of care as received by all participants during the 4 months of the intervention stage of the trial. The data in Table 9.1 was obtained from participants' clinical records, from the completion of the follow-up questionnaires and also from EMIS. Where possible, data from multiple sources was used to check the reliability of the information obtained.

### Medication

As can be seen from Table 9.1, 64.37% of all participants, 67.44% of the collaborative care group, and 61.36% of the usual care group were prescribed medication. The difference between the two groups (6.08%) was not significant ($\chi^2 = 0.205$, $p = 0.65$), nor was there any difference on adherence to medication as rated by the Morisky Adherence Scale (administered at the 4-month follow-up interview) ($t = 0.338$, $p=0.74$). However, it is interesting to note that in both groups adherence was rated as intermediate (scores on the scale range from 0 [high] through to 1 to 2 [intermediate] and to 3 to 4 [low]). As a further indicator of adherence to medication, the number of those participants who returned for at least one further prescription was extracted from EMIS. This showed that 40 out of 56 (71.43%) patients who were prescribed antidepressant medication received at least one further prescription; again there were no differences between the two arms of the trial ($\chi^2 = 0.179$ $p= 0.67$). This suggests relatively good adherence to the protocol in that 20.7% percent of the group had mild depression (that is a score between 10 and 19 on the BDI-II) and would not routinely be expected to be prescribed antidepressants (Anderson *et al*, 2000; Goldberg *et al.*, 2004).

The number of repeat prescriptions offered was in line with other reports of the primary care treatment of depression in Europe (for example, Hansen *et al.*, 2004; Kendrick, 2007) and from collaborative care studies (for example, Unutzer *et al.*, 2002; Miranda *et al.*, 2003).

**Table 9.1: Provision of care to all participants**

| | All participants N= 87[1] | Collaborative care N= 43 | Usual care N= 44 |
|---|---|---|---|
| **Medication** | | | |
| Prescribed (%) | 56 (64.37%) | 29 (67.44%) | 27 (61.36%) |
| Mean Adherence Score (Morisky Scale) | 1.21 (SD 1.14, n=42) | 1.27 (SD 1.20, n=20) | 1.15 (SD 1.09, n=22) |
| More than one prescription in 4-month period (EMIS) | 40/56 (71.43%) | 20/29 (68.96%) | 20/27 (74.07%) |
| **Psychological intervention** | | | |
| Referred | 36 (41.38%) | 20 (46.51%) | 16 (36.36%) |
| Attended | 22 (25.29%) | 12 (27.91%) | 10 (22.73%) |
| **Psychiatric referral** | | | |
| Referred | 3 (3.45%) | 1 (2.32%) | 2 (4.54%) |
| Attended | 2 (2.30%) | 1 (2.32%) | 1 (2.27%) |
| **GP attendances in 4 months** | | | |
| Total | 2.70 (SD 2.87) | 2.72 (SD 3.34) | 2.68 (SD 2.36) |
| Mental health related | 1.72 (SD 2.69) | 1.79 (SD 3.21) | 1.66 (SD 2.09) |

[1] All percentages based on total N unless indicated

## Psychological interventions

Table 9.1 also shows that a total of 36 (41.38%) of the participants in the trial were referred for psychological interventions during the course of the 4 months of the intervention. There was a non-significant difference in favour of collaborative care of 10.15% ($\chi^2 = 0.923$, $p = 0.37$) for referrals to psychological therapies. There was also no significant difference between the two arms of the trial in the percentage of participants

(5.63%) who attended for psychological therapies in the 4-month intervention period of the trial ($\chi^2 = 0.309$ p= 0.59). An examination of the participants' records in the collaborative arm of the trial revealed that 16 out of 22 (72.72%) referred for psychological therapy were referred to the "in-house" practice counsellor. Of the remaining six participants, three were referred to psychological outpatient treatment, two to counsellors outside the practice and one person for family therapy in relation to a problem with their child. Limitations in the data coding and collection systems for the trial meant that it was not possible to obtain this information for those in the usual care group, but given the considerable similarities between the two arms of the trial in the general pattern of referral it may be reasonable to assume that a similar pattern of high referral to the practice counsellor would be found. The number referred to (41.38%) or who received psychological interventions (25.29%) is broadly in line with other collaborative care interventions where psychological interventions were provided as part of the trial core intervention or where referral to psychological interventions was part of the overall trial protocol (for example, Unutzer *et al.*, 2002; Wells *et al.*, 2000).

**GP and psychiatric contacts**

The trial population had an average of 2.7 GP appointments (these were identified from a search of the electronic patient records) in the 4-month intervention period with an average of 1.72 of those appointments having a mental health focus. This equates to approximately 8.1 appointments per year (5.16 for mental health) and is well above the average of 3.5 GP contacts per annum reported in a recent national survey (Hippisley-Cox *et al.*, 2007). There were no differences between the two arms of the trial in consultation rates for all contacts (t = 0.064, p = 0.53) or mental health contacts (t = 0.223, p = 0.82).

The number of referrals for psychiatric assessment was small (3.44%) and below that which might be expected for such a population (Goldberg and colleagues [2004] suggest a figure of around 10% of individuals with depression might be assessed or treated in secondary care ), particularly given the baseline BDI-II score of over 30 for the trial population. This low referral rate may reflect the focus of local secondary mental health services on psychotic disorders. There were no significant differences

between the collaborative care and usual care arm in referrals to psychiatric services ($\chi^2$ = 0.322 p= 0.57).

**Summary**

In terms of the overall provision of care, the use of antidepressants is broadly in line with the agreed protocols although perhaps a little under what might have been expected for a group with depression at the lower end of the severe level. However it should be remembered that the rating of depression severity was taken from a BDI-II score. Adherence was rated as only intermediate, and no differences emerged between the collaborative or usual care groups in terms of either adherence or overall rates of drug use. This raises the possibility that the effect of collaborative care in this trial is unlikely to be due to increased antidepressant use or improved adherence as others have suggested (for example, Gilbody *et al.*, 2006b; Bower *et al.*, 2006). This may be in part a function of the randomisation procedure – as can be seen from the analysis of the semi-structured questionnaire, many participants decide to stop taking medication almost immediately after they had seen the GP, resulting in the intervention being offered after the decision to stop had already been taken. Referrals to psychological therapies (predominantly inhouse counselling) were broadly in line with other collaborative care studies, and no significant differences were found between the two arms of the trial. Again this suggests that the provision of additional psychological therapies did not have a significant impact in this trial. The low rate of referral to psychiatry was surprising given the overall severity rating of depression and may reflect the focus of local services on psychosis. However, this may have resulted in reduced access to specialist advice or treatment (including long-term psychological interventions such as CBT). With the exception of psychiatric referral, the uptake of the interventions is broadly in line with the protocols.

### 9.3 The provision of care by the PCMHWs

Table 9.2 sets out the key elements of the care provided by the PCMHWs in the collaborative care arm of the trial during the 4 months of the intervention phase of the trial. The data is presented for all participants and also for each practice. Differences between the practices are presented as they may allow for a better understanding of problems in adherence to the trial protocols. Table 9.2 shows that 31 (72.09%) of

participants were in receipt of guided self-help. Fourteen (60.87%) in practice 1 and 17 (85.00%) in practice 2 received guided self -help, a difference of 24.13% which, approached significance ($\chi^2 = 3.096$, p= 0.08). The numbers of patients prescribed medication was also different between the two practices: 78.26% for Practice 1 versus 55.00% for Practice 2, but was not statistically significant ($\chi^2 = 2.636$, p= 0.10).

**Table 9.2: Provision of care by PCMHWs**

| Elements of care | Collaborative care[1] N = 43 | Practice 1 N=23 | Practice 2 N=20 |
|---|---|---|---|
| **Number in receipt of guided self-help (GSH)** | 31 (72.09%) | 14 (60.87%) | 17 (85.00%) |
| **Prescribed antidepressant during 4 months** | 29 (67.44%) | 18 (78.26%) | 11 (55.00%) |
| **Medication support** | 25/29 (86.20%) | 15/18 (83.33%) | 10/11 (90.90%) |
| **Number in receipt of both GSH and medication support** | 22 (51.16%) | 12 (52.17%) | 10 (50.00%) |
| **Referral facilitation** | 11 (25.58%) | 4 (17.39%) | 7 (35.00%) |
| **Care coordination** | 14 (32.56%) | 4 (17.39%) | 10 (50%) |
| **Number of contacts with PCMHW** | | | |
| 0 | 1 | 0 | 1 |
| 1 | 7 | 4 | 3 |
| 2 | 5 | 4 | 1 |
| 3 | 10 | 6 | 4 |
| 3+ | 17 | 6 | 11 |
| Inadequate data | 3 | 3 | 0 |
| **Average contacts (SD)** | | | |
| Face-to-face | 2.18 (1.24) | 1.65 (0.75) | 2.70 (1.42) |
| Phone contacts | 1.03 (1.05) | 1.25 (1.12) | 0.80 (0.95) |
| Total no. contacts | 3.20 (1.74) | 2.90 (1.45) | 3.50 (1.99) |

[1] All percentages based on total N unless indicated

This was broadly paralleled by the number of participants receiving medication support (this was determined by whether or not the notes made reference to discussion between the PCMHW and the participant about advice or difficulties concerning the use of medication): 65.21% in the case of Practice 1 and 50.00% in Practice 2, although the percentage of those on medication who received medication support was slightly higher in Practice 2 as a proportion of those on medication (90.90% in Practice 2 as opposed to 83.33% in Practice 1).

Table 9.2 shows that 22 participants (51.16%) received both GSH and medication support, with little difference between the two practices: 12 in Practice 1 (52.17%) and 10 in Practice 2 (50.00%). Overall, 25.58% of participants received referral facilitation, predominantly to services outside the practice. The data was obtained from the case notes and included data on referral facilitation to a wide range of community services including drop-in groups, carers' support groups and benefits advice services. The assistance included telephone reminders, help in attending an interview or advice and discussion about difficulties in attending for such appointments. Although there are almost twice as many examples of referral facilitation from Practice 2 (7; 35.00%) as Practice 1 (4; 17.39%), the overall numbers were small and there was no significant difference between practices ($\chi 2 = 1.742$, $p = 0.19$). In contrast although numbers were again small, the use of case coordination (defined as examples of clear indication from the clinical records of liaison with primary care staff or staff of other services with whom a participant was engaged) was greater in Practice 2 (10; 50%) compared with Practice 1 (4; 17.39%) and this was significant ($\chi 2$ 5.18, $p = 0.02$). In terms of the average number of total contacts, there was also a non-significant difference between the practices with an average of 2.9 (sd1.45) contacts in Practice 1 and an average of 3.5 (sd1.99) in Practice 2 ($t = 1.115$ $p = 0.27$). For face-to-face contacts the difference between the means of 1.05 was significant ($t = 3.086$, $p = 0.004$). There were more telephone contacts in Practice 1 (1.25 [1.12] versus 0.80 [0.95]) but this was not significant ($t = -1.425$ $p = 0.16$).

**Summary**

The data summarised in this section suggest that the PCMHWs were able to deliver the interventions broadly in line with the agreed protocols and 32 out of the 43 (74.42%) participants received at least two contacts with the PCMHWs and 39 out of 43 (90.7%) participants received at least one contact. A broad range of interventions was offered across both practices, with large majorities receiving both guided self-help and medication support. However some differences in the nature of the interventions between the two practices were significant, including the use of case coordination and the average total of face-to-face contacts. Since such differences may contribute to an increased understanding of the implementation of collaborative care in the trial, further practice comparisons are explored below.

## 9.4 Practice differences in the provision of collaborative care

### Psychological therapies

As can be seen from Table 9.3, significantly more participants in Practice 1 received formal psychological interventions, predominantly counselling: 13 (56.52%), as opposed to 3 (15.00%) in Practice 2 ($\chi^2 = 7.894$, p= 0.005). This raises the question whether this might have had some impact on the outcome of the intervention in the two practices; particularly whether the participants in Practice 1 showed any additional benefit given the significantly greater level of psychological interventions. An examination of the primary outcome data, however, does not suggest that this is the case.

**Table 9.3: Use of psychological interventions by the collaborative arm in the two practices***

| | **Practice 1**<br>**N= 23** | **Practice 2**<br>**N = 20** |
|---|---|---|
| **Practice counsellor** | 9 (39.13%) | 1 (5.00%) |
| **Psychology service** | 2 (8.69%) | 1 (5.00%) |
| **External counselling** | 1 (4.35%) | 1 (5.00%) |
| **Family intervention** | 1 (4.35%) | 0 |
| **Total psychological interventions** | 13 (56.52%) | 3 (15.00%) |

*Note the small discrepancies between this table and 9.1 arise from the use of different data sources, EMIS for Table 9.1 and PCMHW records for this table.

The endpoint scores on the BDI-II for the two practices at 4 months are: Practice 1 collaborative care 18.24 (sd12.43), usual care 18.95 (sd14.04); and Practice 2 collaborative care 19.20 (sd12.77), usual care 29.24 (sd14.95). This raises the possibility that any differences in outcome between the two practices could also be due to a lack of improvement of participants in the usual care condition in Practice 2 (they were a more socially deprived group, which may be associated with a poorer prognosis; Goldberg *et al.*, 2004) or because the usual care in Practice 1 was of a better standard. When the data is analysed using the linear mixed effects model with practice as a factor and with baseline BDI-II and employment as covariants, the difference between conditions is still significant (F = 3.061, p = 0.02). The estimated marginal means from this analysis are: Practice 1 collaborative care 15.77 (sd16.74), usual care 21.96 (sd12.86); and Practice 2 collaborative care 16.76 (sd11.76), usual care 25.99 (sd13.69).

This gives a 6.19 difference between collaborative and usual care in Practice 1 and 9.23 in Practice 2.

This raises two related questions: how the increase in psychological interventions occurred and why it was not associated with an increased difference between scores on the BDI-II in Practice 1 over Practice 2. With regard to the increased level of intervention in Practice 1, it is of course possible that this arose by chance but there are a number of alternative explanations. Perhaps most parsimonious is that the resources available at Practice 1 were greater (which was in fact the case). However, this might not entirely explain the difference between the two arms of the trial where there was a significantly greater (60.86% versus 43.47%; $\chi^2 = 7.894$ p= 0.005) use of formal psychological interventions in the collaborative arm.[19] This raises the possibility that there may have been some contamination (Torgenson, 2001); that is, the trial resulted in a change in clinical practice over and above what might have occurred under non-trial conditions. There is some evidence to support this (from reports of the PCMHWs' supervisor); the relationship between the practice-based counsellor and the PCMHW in Practice 1 was initially difficult with the counsellor feeling threatened by the developing role of the PCMHW within the practice and therefore seeking to secure her own position by increasing her activity with trial participants. Of course it is also possible that the increased contact with the counsellor was a result of a planned increase in access to resources. This relates to the second question as to why the increased use of psychological interventions (predominantly counselling) was not associated with an increased benefit in Practice 1. A number of explanations of this are possible. These include an increased rate of remission in Practice 1 (as noted above it had a less socially deprived catchment area) and the possibility that counselling was ineffective (see Chapter 4) for those with moderate or severe depression or that it added little to the benefit already derived from the interventions provided by the PCMHW.

**Review of case notes – nature of the care provided**

An alternative explanation for the possible lack of impact of psychological interventions is that there were differences in the provision of care by the PCMHWs that either

[19] Note that the difference in the provision of psychological interventions is not so marked in the usual care condition with 8 (38%) of Practice 1 participants in receipt of additional formal psychological interventions as compared with 7 (33%) in Practice 2 ($\chi^2 = 0.477$, p= 0.49).

compensated for the lack of psychological intervention or provided additional benefit for the more socially deprived participants in Practice 2. The data presented in Table 9.2 suggested that it was possible that there may have been greater adherence to the collaborative care protocols in Practice 2.

One way of addressing this question would have been to have used a formal measure of adherence to the collaborative care model. Unfortunately the trial included no formal rating of adherence to a model of collaborative care. The Assessment of Chronic Illness Care (ACIC) (Bonomi *et al.*, 2002), which was developed to assess the organisational response to chronic illness, was not judged suitable for the evaluation of the programme because it focused both on wider organisational developments that were beyond the present intervention and chronic physical care, and did not directly address mental health. (Since the initial design of the trial, a patient-related measure, the Patient Assessment of Chronic Illness Care [PACIC; Glasgow *et al.*, 2005] has been developed and although focused on chronic physical health problems it might have been a useful measure in this trial.)

Therefore in the absence of a formal measure of adherence, data from case notes were examined to see if the interventions were provided according to protocols developed for the trial. All case notes were independently reviewed (by the author and the senior clinical psychologist involved in the trial) and a simple classification of the content of the notes (which related directly to the trial protocols) was developed and agreed. This classification was then used to indicate how well the protocols had been followed. The activities of the PCMHWs were classified as follows:

- the provision of advice and support on the use of medication
- the use of guided self-help (including goal setting and behavioural activation – note that simply giving a participant a booklet was not judged to be evidence of its use)
- referral facilitation
- case coordination.

The notes of all the collaborative care participants were then coded (by the author and the senior clinical psychologist) using the classification system above. Where there was

evidence at any point in the clinical records of any of the above activities, a positive response was recorded. In cases were there was disagreement, this was resolved by discussion between the two coders; in practice there were few disagreements.

The results of the case note review are set out in Table 9.4. They are presented for all patients and by practice. The data show that virtually all participants (95.35%) received one or more of the interventions set out in the protocol and there was a very small difference between the two practices (0.65%). Small (that is, less than 10%) and non-significant differences can be seen for goal setting and medication support with a larger (17.61%), but not significant difference, for referral facilitation.

**Table 9.4: Content of collaborative care intervention**

| Content of intervention | All participants N= 43 | Practice 1 N= 23 | Practice 2 N = 20 | p value |
|---|---|---|---|---|
| **Guided self-help** | | | | |
| Goal setting | 15 (34.88%) | 7 (30.43%) | 8 (40.00%) | n.s.[2] |
| Behavioural activation | 12 (27.91%) | 3 (13.04%) | 9 (45.00%) | p = 0.02[2] |
| Specific strategies | 19 (44.19%) | 5 (21.74%) | 14 (70.00%) | p = 0.001[2] |
| **Medication support**[1] | 25/29 (86.21%) | 15/18 (83.33%) | 10/11 (90.91%) | n.s.[2] |
| **Referral facilitation** | 11 (25.58%) | 4 (17.39%) | 7 (35.00%) | n.s.[2] |
| **Case coordination** | 14 (32.56%) | 4 (17.39%) | 10 (50.00%) | p = 0.02[2] |
| **Received any of above interventions** | 41 (95.35%) | 22 (95.65%) | 19 (95.00%) | n.s.[2] |

[1] Note only 29 participants were prescribed medication, comprising 18 in Practice 1 and 11 in Practice 2. [2] Chi-squared test used.

However, three activities (behavioural activation, specific strategies (such as relaxation techniques, graded exposure and thought records)) and case coordination) were significantly more frequent in Practice 2. This may substantiate the suggestion that some of the difference in outcomes between practices may be related to a greater adherence to the protocols in Practice 2.

**Summary**

A review of referral practices and the content of the clinical notes of the PCMHWs identified a number of differences in the nature of the interventions offered in the two practices being identified with more evidence of collaborative care interventions in Practice 2. It should be noted that the effect of the collaborative care intervention was greater in Practice 2 (when baseline unadjusted and estimated means are compared). There are a number of possible explanations for this, including a higher remission rate in Practice 1, but an increased use of collaborative care interventions may also have contributed.

## 9.5 Participants' response to the provision of care by the PCMHWs

### Participants' views of the self-help materials

Table 9.5 summarises participants' responses to the self-help material provided by the PCMHWs during the 4 months of the intervention stage of the trial, which were taken from the follow-up questionnaire. For ease of presentation and analysis, responses were generally collapsed into positive (1 and 2) or negative ratings (4 and 5).

As can be seen from Table 9.5 the results of the follow-up questionnaire are a generally positive endorsement of the material provided with the majority of participants having read some of the material (overall 58.82% ) and finding them easy to use (70.59%). There were no major differences in the use of the various booklets between practices although it is interesting to note that the most commonly used booklet was *Stress and Anxiety* and not *Depression*. This may reflect the quality or nature of the booklet but also the fact that there is considerable comorbidity of anxiety and depression (Melmartin *et al.*, 2002) and the possibility that some people would not wish to see themselves as depressed, perhaps preferring the more acceptable term "stress". Although there was a generally positive response, a significant number (between 11.11% for the depression booklet and 31.25% for the panic booklet) did not find them helpful. This suggests that thought should be given to redesigning the booklets or possibly more selective use of them.

**Table 9.5: Participants' views of the self-help materials**

| | All | Practice 1 | Practice 2 |
|---|---|---|---|
| **Received self-help booklets** | **N = 34** | **N = 20** | **N = 14** |
| **Read (more than half or all)** | 20 (58.82%) | 12 (60.00%) | 8 (57.14%) |
| **Ease of use (extremely or quite)** | 24 (70.59%) | 15 (75.00%) | 9 (64.29%) |
| **Use of exercises in booklets** | | | |
| Yes (freq/quite often) | 5 (14.71%) | 4 (20.00%) | 1 (7.14%) |
| Yes (occasionally) | 15 (44.12%) | 9 (45.00%) | 6 (42.86%) |
| No | 14 (41.18%) | 7 (35.00%) | 7 (50.00%) |
| **Individual booklets** | | | |
| **Antidepressants** | N=17 | N=12 | N=5 |
| Helpful (1-2) | 10 (58.82%) | 7 (58.33%) | 3 (60.00%) |
| Not helpful (4-5) | 3 (17.65%) | 2 (16.67%) | 1 (20.00%) |
| **Depression** | N=27 | N=16 | N=11 |
| Helpful (1-2) | 18 (66.67%) | 11(68.75%) | 7(63.64%) |
| Not Helpful (4-5) | 3 (11.11%) | 1 (6.25%) | 2 (18.18%) |
| **Stress and anxiety** | N=24 | N=13 | N=11 |
| Helpful (1-2) | 14 (58.33%) | 8 (61.54%) | 6 (54.55%) |
| Not helpful (4-5) | 4 (16.67%) | 1 (7.69%) | 3 (27.27%) |
| **Panic** | N=16 | N=8 | N=8 |
| Helpful (1-2) | 10 (62.50%) | 5 (62.50%) | 5 (62.50%) |
| Not helpful (4-5) | 5 (31.25%) | 2 (25.00%) | 3 (37.50%) |

## Participants' views of the PCMHWs

Table 9.6 sets out participants' views of the service provided by the PCMHWs (other than the self-help materials) during the 4 months of the intervention stage of the trial, which were taken from the follow-up questionnaire. As with the data on guided self-help, responses were collapsed into positive (1 and 2) or negative ratings (4 and 5) for ease of presentation and analysis. Participants were generally positive about the interventions provided by the PCMHWs with the helpfulness of contacts and understanding of problems scoring around 80% for all participants and in both practices. (This is in line with the formal satisfaction rating on the CSQ-8 in Chapter 8.) There

was a less positive response concerning the number of contacts with PCMHWs (with around only 65% satisfied), with a significant number (around 21%) saying that they would prefer more contacts. The duration of the meeting—typically no more than 45 minutes for the first appointment (and no more than 30 minutes subsequently)—appeared to be satisfactory (around 79%). However, there was less positive endorsement of telephone contacts with only 50% saying that they found them helpful.

**Table 9.6: Participants' views of the PCMHWs**

| | | All | Practice 1 | Practice 2 |
|---|---|---|---|---|
| **Contact helpful** | Extremely helpful and somewhat helpful | 27/34 (79.41%) | 15/19 (78.95%) | 12/15 (80.00%) |
| **Problems understood** | Very much/ moderately | 27/33 (81.82%) | 15/19 (78.95%) | 12/14 (85.71%) |
| **Would materials be as useful without PCMHW?** | Def not/ probably not | 18/33 (54.55%) | 12/19 (63.16%) | 6/14 42.86%) |
| **Number of contacts** | Happy | 22/34 (64.71%) | 11/19 (57.89%) | 11/15 (73.33%) |
| | Prefer more | 7/34 (20.59%) | 4/19 (21.05%) | 3/15 (20.00%) |
| **Duration of meetings** | Long enough | 27/34 (79.41%) | 15/19 (78.95%) | 12/15 (80.00%) |
| | Too short | 5/34 (14.71%) | 2/19 (10.53%) | 3/15 (20.00%) |
| **Telephone contacts** | Extremely helpful/ somewhat helpful | 17/34 (50.00%) | 9/19 (47.37%) | 8/15 (53.33%) |

## Summary

The overall response from the follow-up questionnaire to the PCMHWs was positive. Self-help materials were used and valued by the majority although a majority also said that the materials would have been less useful without the assistance of the PCMHW. Some of the self-help materials such as the panic booklet had a considerable percentage of negative ratings (31.25%). Participants reported that they felt their problems were understood and they were content with the face-to-face contacts but were less happy with the telephone contacts. The results suggest that the protocols for a future trial may

need adjusting with more discriminate use of some of the booklets and the use of face-to-face contacts. The content of some of the booklets may also need revision.

**9.6 Participants' views of their care - the semi-structured questionnaire**

Participants' views of the services delivered in the trial were also obtained from a semi-structured questionnaire (see Chapter 7, Appendix P). The questionnaires were delivered either by postal interview and returned, or participants were interviewed face to face or over the telephone. (Only patients receiving collaborative care were asked questions concerning PCMHWs and guided self-help.) A total of 54 patients returned the postal questionnaires and a further 15 patients were interviewed directly. The overall response rate to both the interviews and the postal questionnaires was 79.31% (69 out of 87); 34 responses were received from the collaborative care arm and 35 from the usual care arm. This represents a reasonably good response rate with an even distribution between both arms.

The data was analysed using the modified framework approach following the procedure outlined by Ritchie and Spencer (1994). The author and the senior clinical psychologist from the trial steering group read each questionnaire/transcript individually and identified emerging themes before discussing the responses together and reaching a consensus on the grouping of themes to develop an overall thematic framework. The framework was then systematically applied to each response and the themes identified. Themes were based both on the review of the responses and *a priori* reviews of what might be relevant and important from previous studies of collaborative care (see Chapter 2).

The following themes were identified:

1. The value and tolerability of antidepressants
2. The role of the GP
3. The coordination of care
4. The support provided by the PCMHW
5. The value of guided self-help.

As can be seen from the questionnaire (see Chapter 7, Appendix P) questions were asked about whether the intervention led to a better understanding of the person's

problems. However, because few substantial responses were received to these questions, it was not possible to identify any significant themes.

*The value and tolerability of antidepressant medication*

There was considerable variation in views between participants in both the collaborative care and usual care arms about the use of medication. A significant number of participants reported that antidepressant medication was helpful. For example, one patient in the collaborative care arm said:

> *"Yeah it's been very helpful actually. It's really helpful, so far so good... I started the actual course of antidepressants so it took me a week or so to actually kind of kick that habit and then feel kind of confident enough to actually think that I could go into the antidepressants, which is what I did, and um I've gone through my first 28 days of that so, so far so good."*

Another in the usual care arm said:

> *"Medication was most effective; I suffered no side effects. Antidepressants started to take effect within a few days."*

However, a significant number of individuals raised concerns about the medication and a number reported stopping. Some referred to fears of becoming dependent or said that they did not wish to continue taking medication and a number did not start medication because of concerns about side effects.

> *"I was prescribed antidepressants in May and I decided not to start the course as I have a fear of becoming dependent on these."* (Usual care participant)

> *"I don't like pills; I think they don't do your body much good. I think you ought to be able to reason yourself out of things. I have a limited, not personal experience, but a little experience of Seroxat which is addictive or it's not addictive, but you can't come off it because it gives you such dreadful symptoms."* (Usual care participant)

> *"I stopped taking antidepressants because of the side effects, like feeling sick and losing my appetite. I am trying not to take medication; I am trying to help myself without medication."* (Collaborative care participant)

Overall there tended to be more positive statements (or at least less negative statements) regarding the use of medication in the collaborative care group and specific reference to support from the PCMHW.

> *"Very good actually, very good. I saw [the PCMHW] downstairs on a couple of occasions. Again, I would have liked to have seen her, seen more of her but I just found ...it was enough for me to come to terms with the whole situation of taking the antidepressants."* (Collaborative care participant)

> *"The reassurance that I would not have antidepressants forced on me and would be offered alternatives."* (Collaborative care participant)

*The role of the GP*

Comments from participants about their GPs tended to be positive on the whole. This was true for both arms of the trial, but was perhaps more strongly emphasised in the usual care arm, which was not surprising because for some participants GPs were the sole providers of care.

> *"[The GP] went through each issue as it came up and offered encouragement and help. She was also usually available to see me when I needed it."* (Usual care participant)

> *"I think the doctors were very helpful..... they didn't make me feel as if I was being stupid in coming in, um, which I did feel because I'm of the opinion that one doesn't really need counselling, one can just sort of wait and work it all out for oneself."* (Usual care participant)

The comments also suggested that the participants not only felt that the GP helped by organising care or prescribing antidepressants, but that they were both supported and understood.

> *"Somebody was there who understood my mood and listened to me and advised me how to move on in my life".* (Collaborative care participant)

*The co-ordination of care*

Participants, particularly in the collaborative care arm where one would expect things to be more positive, were generally positive and complimentary about the organisation of service and the way things were brought together.

> *"The whole experience, I felt understood and cared for. I felt supported and that someone was bothered about me – this alone reduced the need I felt to actually talk to someone. I felt instantly better once I knew someone was bothered I wasn't feeling good."* (Collaborative care participant)

> *"And the phone calls were really good ..... I really needed that phone call, just the reassurance that someone's there kind of thing, cos I did feel very alone because it would be a bit of a gap between the next time I would see [PCMHW] but, but I had that phone call so I could talk to her and there was a time when I said 'look [PCMHW], I'm just gonna kill myself you know, that's how I feel' and you know, she would say look don't do anything rash, go and see [GP]."* (Collaborative care participant)

> *"I like the way how [PCMHW], Dr. X they all interacted and stuff and like um, yeah I enjoyed, I did like that."* (Collaborative care participant)

In contrast, there were relatively fewer positive comments about case co-ordination in the usual care group and also a number of related complaints about the waiting time for treatment and the lack of alternative services.

> *"I am disappointed that I was left to my own devices when I have been feeling particularly vulnerable, helpless and self-destructive."* (Usual care participant)

> *"What would be helpful I think is if you had somebody in the surgery where you could say well I want to see that person because ... you know I need to talk to somebody, ... again who's not in the medical profession .... But I mean somebody who's really basically, is prepared to sit and listen to what you've got to say."* (Usual care participant)

Where individuals in the usual care arm were positive about coordination, it was usually attributed to the GP.

*"I think my GP, Dr. X, has been great (and even Dr. Y, when Dr. X was away I could see Dr. Y) they've be really kind and really understanding, very understanding, very caring and... I have been very lucky that I have had this support and I feel that if I didn't have this support I pretty much know that I would have done something to myself, I would have harmed myself".* (Usual care participant)

*The support provided by the PCMHW*

Participants' views of the PCMHWs were also generally positive. The opportunity to talk about their difficulties with the PCMHW was welcomed, and participants were generally very positive about the knowledge and information given.

*"Just someone to talk to really, which I found very useful because you tell your family... and they go 'Oh, just get on with it' you know, sort of attitude, which family do do I know. And so it was, it was good to talk to somebody else.... I found that useful."* (Collaborative care participant)

*"I really liked [the PCMHW]'s part of the service, and when I would see her .... I really enjoyed those; I didn't actually want it to end. She was really understanding, really caring and she was so encouraging."* (Collaborative care participant)

*"... she would say 'well, look how far you've come since I first met you' and she was just so encouraging and then I would say 'oh, I've failed to do this task' and then she would say 'well look at your other list and look at all the other ticks you've done and you've achieved and she would say I would only be able to achieve one and you've done about six' and she was so encouraging."* (Collaborative care participant)

However, a number of participants raised doubts about the age and experience of their PCMHW.

*"The young woman I saw was very nice but looked 18 and I am a 60-year-old professional. I felt she couldn't help me almost as soon as she started talking. The counsellor, probably 40ish, had more life experience and was excellent."* (Collaborative care participant)

*"The person who saw me once and subsequently phoned me several times looked and seemed extremely young. I found it difficult to relate to her because of her age."* (Collaborative care participant)

*The value of guided self-help*

The comments on guided self-help were varied. There were a number of positive comments and these often centred on structure and direction provided, for example in encouraging participants to keep an activity diary.

*"I made a little diary where I kept my daily thoughts and to do list which I was really proud of, I mean I loved showing her my booklets. I used to love talking about the booklets cos she gave me three booklets when I first met her and then the second time I met her she was shocked that I did the whole three booklets ... you know I enjoyed doing it and just.. she went through the exercises, like, I didn't understand how to do graded practice, cos when you read its hard but when you apply it it's difficult applying it in practice and so ...we went though a graded practice and we did it together like ... and then, you know just all these different steps which I would've never thought of properly before and just things like that and problem solving like giving me other options and looking at the brighter side".* (Collaborative care participant)

*"I found the booklets to be very well written because they could be understood by someone with quite a low reading age but were also not patronising for someone with a higher reading age."* (Collaborative care participant)

However, a number of people had doubts about the booklets, feeling that they were not suitable to their needs and that the materials were too limited and more input was needed or that a person might be too depressed to use them properly. Others found the diaries not really relevant to them, suggesting that they might be more appropriate for people with longer-term depression.

*"I thought a lot of them were a little bit ... it was like they were talking to people that kind of had a long experience of depression for example, whereas myself it was a first my first situation ...I felt it was a little bit full of... for someone who had just come in you know to this situation, realising they actually were depressed that's why they were*

*feeling the way they were. I think it didn't really help me as much as it could have done.*" (Collaborative care participant)

*"Face to face, fine, I can handle that but actually sitting down with a book and reading it, no. I did glance through it and I thought, no I'd rather talk to someone."* (Collaborative care participant)

*"Yes, booklets that are given, most of the people can't concentrate and don't/can't read them, that's why they may not know the cause of depression and how to cope with it."* (Collaborative care participant)

*Summary of the responses from the semi-structured questionnaires*

The outcomes from the semi-structured interviews are broadly consistent with the results from other parts of the process evaluation. The role of the PCMHW in coordinating care, explaining about treatment and being available to the participants was valued. There was general satisfaction with the GP and a clear suggestion, particularly in the usual care group, that the relationship with the GP was important. There was less emphasis on this aspect in the collaborative care group, which perhaps relates to the need to develop an alliance in the treatment of depression. The use of collaborative care may allow the alliance to develop not just with the GP. In some circumstances this may make it possible to engage and retain people who otherwise would not engage with treatment. There was ambivalence and uncertainty about medication, but a number of people were also very positive about it.

There was some feeling that both the duration and frequency of contacts could have been greater and this is something that might be considered in the adaptation and development of the model. In addition, people were generally positive about guided self-help, but the emphasis was often as much on the activities emerging from the intervention as on the booklets themselves. A number of people however felt that the booklets were a little too simplistic and did not directly address their problems. A number of people also mentioned the age of the PCMHWs (two of whom were young women in their mid 20s), and that this presented a barrier to full engagement or some people's engagement.

The findings from this small qualitative study are in line with a larger qualitative study of PCMHWs undertaken by England and Lester (2007), which suggested that integration of PCMHWs into the care system and the delivery of rapid support were valued by patients. England and Lester emphasised the tension of providing the role in a setting where patients' and practitioners' expectations may be very different. As in this trial, the personal support provided by the PCMHW (for example, the opportunity to talk about problems) was highly valued.

### 9.7 The perceptions of practice staff – outcomes of the focus groups

In order to obtain a view of the collaborative care intervention from the two general practices that participated in this trial, it was the intention to hold a focus group in each practice comprising the GPs, administrative staff and other clinical staff such as practice nurses and counsellors. While this was achieved for Practice 1 (five GPs, the practice counsellor and the practice manager), only three participants (a single GP, the practice manager and a receptionist) were able to attend from Practice 2. This limited the information that could be obtained, but the results of that meeting are nevertheless briefly summarised below.

The focus groups followed a common method with a set of predetermined questions directed at both groups (see Appendix Q). The focus groups were conducted by an independent senior psychologist who was familiar with the trial but had no role in the research programme. The details of the two groups are presented below for each practice. The purpose of the focus group was not only to explore practice staff views of the interventions itself but also of the impact of the research on the practice, participants and the feasibility of the research. The groups were tape recorded, the outcome was transcribed and the transcripts examined. The analysis was undertaken by the author in consultation with the senior psychologist who reviewed the individual interviews. Given that there were only two focus groups, and one had a very limited membership, no formal thematic analysis was undertaken.

#### Practice 1

This focus group was attended by five GPs, the practice manager, and the practice counsellor. In this practice one of the major comments to emerge was the increased workload on the practice; for example one GP said:

*"We think it created work, it's an observation. I mean it is probably good in the sense that we were finding people with depression or maybe it fished out some people who perhaps we would not know about".*

This was supported by a further GP:

*"It certainly did that – it brought out some people who were really quite unwell, especially some older men who came".*

Although this was perceived as positive, it was recognised that a significant part of the additional work fell, not to the PCMHW, but to the GP. It was also made clear by the focus group that the intervention imposed an increased workload on the counsellor. There was concern among the GPs that the use of the flyers led to an increased number of people contacting the practice for depression but who made no reference to the flyer or the trial. They also thought an increased number of people had approached the practice who did not have depression but other psychological or physical problems.

GPs were also unhappy about the way in which the content of the flyer was developed, and felt that the discussion of this was not well handled by the research team. For example:

*"I felt that it was almost as if we were being told, we were being too pernickety, you know. The other practice had not complained about it and it hadn't been an issue with us and it had got though the ethics committee and everything".*

GPs also had concerns about the way the service was presented to individual patients; they felt that the flyer suggested the possibility that a new service was available to them, when in fact they only had a 50% chance of receiving the service. The way the flyers were worded was potentially misleading and this presented some dilemmas and awkwardness for the GPs.'

*"I thought that definitely for me that it* [the flyers] *brought men that wouldn't have come in, but not necessarily for depression. They said "Oh I thought should come and see you because I got this letter. I'm not depressed but oh..."*

They also raised concerns about the impact of the trial design, for example one GP said:

*"I think the randomisation was the thing that we struggled with most."*

The GPs felt that, given the brevity of the intervention, the actual assessments conducted as part of the research might also have had a beneficial effect, for example one GP said:

> *"But I actually have to say...that I also think that the research assistant is extremely good and that the intervention is like having a diagnostic interview, lots of people just got randomised and found that very therapeutic actually."*

There was also some suggestion that patients were confused about the various roles of staff in the practice, for example the counsellor said:

> *"I spoke to lots of patients who were also seeing the primary care worker and it could have been very complicated because sometimes patients were confused about our different roles, but she was so good and also such a good communicator that problems that might be potential were ironed out."*

GPs and practice staff also talked about other potential benefits of the programme, for example the counsellor said:

> *"I think that it heightened our awareness of self-help materials, we put them on our computer screens and it's the kind of thing to have on hand to dip into immediately."*

GPs felt that the programme had an overall benefit on the practice:

> *"I think probably over the last year we have probably had an increased profile of depression. I am sure that quite a lot is to do with the study. It is an increased profile, I think the question is how many increased profiles can we sustain at any one time?"*

Although the GPs rated the value of the overall programme they were uncertain about whether it added additional benefit and whether it could be rolled out to a range of other practices. They had quite a significant debate about whether collaborative care should be expanded or whether it would be better to take on a graduate worker (PCMHW) who could focus on the provision of guided self-help to a range of disorders in addition to depression; for example, one GP said:

> *"It is interesting to me. That's a very interesting point because you decide, I mean you would. Do you think enhanced care studies are a good idea for the future? But I mean you are raising an important issue and I am a bit like you, I'm not sure maybe a graduate worker would be better".*

Another GP commented:

> *"I mean we should not be looking at this as therapy I think it would be better for say chronic depression rather than new cases of depression, but that's a different point".*

**Practice 2**

The focus group at Practice 2 was poorly attended, with only one GP, the practice manager and a senior receptionist. In contrast to Practice 1, this practice did not think that there had been a major impact of the research on their workload. The GP felt that it was helpful to have the PCMHW in the practice, but, as noted above, there was some disappointment in the impact of randomisation in terms of the patients who did not receive collaborative care. In contrast with Practice 1, they thought that flyers were positively helpful, although they did raise concerns about the possibility of other individuals opening up the flyers and finding that the individual had a history of mental illness or a chronic physical health problem. They also felt that this process did not uncover many new patients, but triggered a number of older patients into coming back and seeking further help.

The GP felt that the trial had generated further work and that the PCMHW's time might have been better spent in supporting practice patients with severe mental illness in maintaining contact with the secondary care mental health services. The practice was also concerned that there would be no long-term funding for the collaborative care initiative and that it would generate a lot of work for no long-term benefit.

**Summary of the focus groups**

Although the information obtained from Practice 2 was very limited, the focus groups nevertheless provided some important information about the trial that may inform a future study. GPs were concerned about increased workloads, but also grateful that more patients with depression were identified. The GPs also raised some concerns about the impact of the research design on their practice including the randomised procedures and the leaflets. In both practices there was uncertainty about the benefit of the intervention and whether the resources might be put to other uses, such as emphasing more direct treatment or supporting links with secondary care. However, increased awareness of depression and the usefulness of the self-help materials were identified as a possible benefit. Important pointers for a further trial emerged, including greater discussion of workload, the impact of research on the practice and exploration of the role of the PCMHW in relation to the overall work programme of the practice.

### 9.8 Overview – effective delivery and monitoring of the interventions

The process evaluation demonstrated that it was possible to provide the interventions as specified in the trial protocols, including the delivery of guided self-help, medication (and medication support), case coordination and referral facilitation. The procedures for obtaining these from case notes and the electronic records of the practices worked well. Adherence to the protocols using formal rating scales and examination of the case notes was also reasonable. Completion rates for individual outcome measures were good for health service research and comparable to similar studies with an average completion rate of 80% (range 75 to 85%), with all but two measures in both arms of the trial achieving 80% or greater completion.

There was some variation in the uptake of guided self-help. Participants were generally positive about the interventions, but some were less satisfied with the guided self-help materials (for example, the booklets on panic). There was general satisfaction with the role of the PCMHWs, particularly in offering an opportunity to discuss problems and in providing some general support and structure to the care delivered. Participants were generally positive about the support received from their GPs. Some differences emerged between the practices, which suggests that the procedures for delivering and monitoring the intervention may have some validity. The outcome of the focus groups suggests that GPs had concerns about increased workload and the constraints on the practice imposed by the research.

The results of the process evaluation raise some questions about the relative value of the guided self-help, additional psychological therapies, the use of psychiatric services and the value of medication. It is interesting to note that the difference in the psychological interventions between the two practices was not associated with a difference in outcomes, and that the uptake and adherence to medication was not different between the two arms of the trial, which is not what one might have expected from previous reviews (for example, Gilbody *et al.*, 2006)

The trial also has implications for the delivery of future interventions, including: redesign of the self-help materials; a more discriminating use of the self-help materials; and more prompt delivery of medication support. The need for further discussion with clinical staff about the possible impact on workload and the problems of randomisation

was also identified. The possible contamination noted in Practice 1 also suggests changes to the trial design. Perhaps with clearer protocols for the use of additional psychological therapies as have been developed in some collaborative care trials (for example, Miranda *et al.*, 2003)

The effective implementation and evaluation of collaborative care demanded a number changes in the practices including: incorporation of a new staff role, changes to referral and identification systems, and development of case coordination protocols, all of which had to be in place for the trial to be successful. The trial demonstrated that this was possible, although considerable preparation work (approximately 6 months) was needed to establish the new systems in the practices. The results of the process evaluation suggest that a large-scale trial of collaborative care is feasible, and that many of the interventions and measures used in this feasibility trial could be developed and adapted.

### 9.9 Limitations

The process evaluation of the trial had a number of limitations. The lack of a formal rating of adherence such as the PACIC (Glasgow *et al.*, 2005) leaves some uncertainty about the integrity of the intervention delivered. In addition, although the competence framework was developed as part of this thesis and helped to underpin the work on low intensity interventions by specifying the competences required it could have been used to develop a formal adherence measure. As noted above there was evidence of variation in the delivery of low intensity interventions between practices with some suggestion of greater adherence by the PCMHW in Practice 2 in contrast to either of the PCMHW in Practice 1. (This may have been related to the superior outcomes in Practice 2). However, this observation is based on an examination of the clinical records; the use of a formal measure of adherence developed from the competence framework could have provided a more secure basis for this observation. For the qualitative analysis of patient interviews, although the sample used in the qualitative interviews was small and the transcripts/responses were limited, the lack of a formal rating of inter-rater reliability of the coding may be questioned. A number of measures such as medication adherence also relied on self-rating and an external validation of this might have been helpful. The use of both electronic patient records and clinical records of the PCMHWs generally helped in validation of the data but differences in coding systems and different time

scales (for example, electronic record reviews covered the full 4-month intervention period whereas the duration of contact with the PCMHW may have been less than 4 months) may have limited the value of comparisons of the two data sources. In addition, the experience of the PCMHWs was not formally assessed, although given the small number involved (three individuals in two posts) the value of this may have been limited. The process measures included lacked a measure of the alliance and this might have been helpful in further refining the design of the intervention. Although the differences in psychological interventions offered between practices and the lack of a difference in medication uptake or adherence was noted, the low numbers involved in the trial should caution against drawing firm conclusions. Finally, there was limited information available on those who had dropped out of treatment; the views of this group concerning the intervention may have been particularly informative.

# 10. Discussion

## 10.1 Introduction

At the outset, this thesis considered the problems faced in identifying and delivering effective treatments for depression, recognising that current routine care for depression is often sub-optimal (Donoghue & Tylee, 1996; Goldberg *et al.*, 2004). The response of evidence-based medicine to this challenge was discussed, the commonly used tools of evidence-based medicine (such as systematic reviews and clinical guidelines) were reviewed, and the implications of drawing on an international evidence based were considered. In particular, the challenge of transferring complex interventions between different healthcare systems was discussed. The thesis focused specifically on collaborative care programmes for depression that have been developed in the US, and examined whether collaborative care could be an effective intervention in the UK healthcare system. The consistent results from the US (Gilbody *et al.*, 2006b; Bower *et al.*, 2006) suggested that collaborative care was effective, although uncertainty about its effectiveness in the European or UK context (for example, Mann *et al.*, 1998; Smit *et al.*, 2006) suggested that caution was required before the wholesale adoption of collaborative care as advocated by some leading authorities (for example, Simon, 2006). The issue of its cost effectiveness (Gilbody *et al.*, 2006b) and comparative effectiveness with other ways of delivering enhanced care for depression such as the *attached professional model* (Cape *et al.*, 2007) were also discussed.

The evidence for the effectiveness of collaborative care, together with reviews of pharmacological and psychological interventions for depression, informed the development and implementation of an exploratory trial of collaborative care in a UK primary care setting. This chapter focuses on the outcomes of that exploratory trial, including the content of the collaborative care intervention and the trial design, and considers these outcomes for the theory of collaborative care, its development in the UK and the design of a large-scale definitive trial of collaborative care in the UK.

## 10.2 Trial outcomes

The primary outcome measure used in the trial was depressive symptomatology at 4 months (that is, at the end of the intervention phase). It was also reported at 8 months.

At 4 months the results were significant and at both time points the reported effect sizes were of a moderate size (Cohen, 1988), in excess of those reported in the meta-analyses of collaborative care and towards the upper end of reported outcomes for any reported study of collaborative care (for example, Bower *et al.*, 2006; Gilbody *et al.*, 2006b). Given that the comparator was standard primary care services in two well-established group practices, this confirms that the first aim of the trial identified in Chapter 7 (developing and testing the intervention against an appropriate comparator) had been achieved. The results on secondary outcome measures, with the exception of satisfaction, were not as positive but might reflect the choice of measures as much as a lack of effect (this issue will be addressed in the discussion about measures below).

A further aim of the trial was to test the acceptability and relevance to clinicians and patients of the organisational changes in collaborative care. Again, the results were generally positive, with increased satisfaction with the collaborative care intervention from participants. However, clinicians (GPs) had concerns about increased workload and some questions about the other possible roles for the PCMHWs (for example, whether they would concentrate solely on providing guided self-help or have a wider mental health liaison role with secondary care mental health services). Clearly this may require further testing in a large-scale trial, but no significant objections to the broad approach were identified in this trial. Participants were also generally satisfied with the interventions delivered, although some aspects of the interventions, for example the use of telephone calls and some of the booklets used in the guided self-help, were not positively rated by a substantial minority of the participants.

Based on the effect size obtained on the primary outcome measure, a power calculation indicates that a larger-scale definitive trial would require approximately 200 participants (that is 100 participants in each arm of the trial) to have 80% power of detecting a difference at the 0.05 level of significance.

### 10.3 Trial design

Key elements to be tested in the trial design were the recruitment and retention strategies. As can be seen from Chapter 8, although there was an over-estimate of the rate of presentation of new cases of depression, the recruitment strategies proved successful, in particular GP referrals and the flyer for people with previous episodes of

depression. The lack of information about some patients who were identified as depressed, in particular those withdrawn by the GP, is a limitation of the study. Retention in the study was acceptable and well within the limits of other comparable studies, but more assertive follow-up (perhaps more feasible in a well-resourced large-scale trial) would bring more confidence to the results. The acceptability of randomisation to participants was not directly and formally tested, but a number of potential participants may have withdrawn when they became aware of it. For example, a number of participants in the usual care arm expressed disappointment at not being randomised to collaborative care in the semi-structured questionnaires. Some of the more strident criticism of the randomisation process came from the GPs in the Practice 1 focus group. They expressed unease when making a referral to the trial because they thought it might mean a less appropriate intervention being delivered to those receiving usual care. This could have impacted on referral rates to the study. It may be that more regular contact with the GPs and more information on the uncertainty associated with use of collaborative care in an NHS setting would have addressed these concerns. But other more significant changes to trial design may need to be considered, including a cluster randomisation approach, which would remove the need to allocate individual patients. This would eradicate the problems associated with individual randomisation but would generate others, including the inflation of the power calculation to take account of the intra-cluster correlation coefficients (ICC) (Hayes & Bennett, 1999), and the increased difficulties associated with recruitment in cluster randomised trials in the comparator or usual care arm (Farrin *et al,* 2004).

The completion rates of the primary and secondary outcomes measures and the follow-up questionnaire were within acceptable limits. There was no major variation in the rates of completion between questionnaires, which suggests that participants did not find any particular questionnaire less acceptable (for example, completion rates varied from 100% to 97.73% at baseline and 82.70% to 79.31% at 4 months). However, of more concern was the potential lack of sensitivity to change of some of the measures. The BDI-II and the CSQ-8 appeared sensitive to change, as did the mental component score of the SF-12 at 4- and 8-month follow-up and for the sub-group analysis of moderate to severe depression. However, this was not the case for the physical component score of the SF-12 (perhaps not surprising given the disorder under

investigation was not a physical one) and the WSAS. The lack of a consistent finding could of course stem from the fact that the intervention, which was relatively short term, had little impact on work and social adjustment; (note the claim of Mundt and colleagues (2002) that the measure is sensitive to change). This suggests that consideration might be given to other measures of social and personal functioning such the Social Adjustment Scale – Self Report (Weissman & Bothwell, 1976), which has been used in a number of studies of depression (for example, Elkin *et al.*, 1989) and collaborative care (for example, Miranda *et al.*, 2003). However, both measures take longer than the WSAS to complete and this may affect acceptability to participants.

Although because the small sample size, the trial did not assess the cost effectiveness of the intervention, consideration could have been given to assessing the feasibility of collecting data such as psychometric measures of quality of life (for example, EQ-5D [EuroQoL Group, 1990]) or cost-utilisation data (for example, The Client Service Receipt Inventory, Beecham & Knapp, 2001), which may more easily facilitate the development of cost-effectiveness measures. This is important because the question of cost effectiveness is likely to be central to the adoption of collaborative care in a UK setting.

It should also be noted that there are several other methodological limitations of the trial, including non-blinded research assessments at follow-up, the use of GP diagnoses and the lack of formal diagnostic assessment of participants, all of which could contribute to bias in the assessment of the trial outcomes. A number of other limitations in the use of measures in the trial have been identified. Improvements could include: using non-self-report measures of medication compliance (although patient reports of compliance are generally held to be reasonably reliable [Katon *et al.*, 1996]); ascertaining participants' experience of the research process; determining PCMHWs' experience of the intervention; providing a fuller description of the content of the usual care intervention; and using adherence measures for the PCMHW delivering the low-intensity psychological interventions. Perhaps more importantly in terms of the overall trial design, formal measures of the organisation of care both from a patient perspective, for example by the use of the PACIC (Glasgow *et al.*, 2005) or a modified form of the ACIC (Bonomi *et al.*, 2001), would have been desirable. Such measures would give an

indication of the degree of adherence to a preferred model of collaborative care. A specific measure of communication between those delivering the interventions and other members of the primary care team such as GPs may also be required. Refining and using these measures should contribute to a fuller description of the care provided in the comparator arms of any future trials.

### 10.4 Delivering the effective components of a collaborative care intervention

A key question for this thesis was whether it was possible to develop an intervention that delivered the key elements of a collaborative intervention and did so in a way that was compatible with the UK healthcare system (Hawe *et al.*, 2004).

#### The elements of collaborative care

The process evaluation demonstrated that the trial was capable of delivering most of the patient-focused elements of collaborative care. If the four essential elements of the chronic care model as identified by Von Korff and colleagues (1997) are considered[20], adopting a guided self-help approach and developing a role in the coordination of care, the intervention (through its focus on a collaborative, patient-defined approach to specified problems) achieved three of the key elements. The fourth (the provision of active and sustained follow-up) was not fully met, due partly to the limitations of the protocols adopted for the intervention and also to the nature of the exploratory trial design. Examination of individual case records offered evidence of care coordination, but it was not the case that the PCMHW took on the full coordination of the care; that remained with the GP. This is both understandable and advisable, given the relatively short contact time that the PCMHW had with participants. It may also require a significant change in the role of GPs for the collaborative care model to be fully developed in a UK setting.

In addition to the patient-focused aspects of collaborative care, a number of organisational elements were also identified as important elements of a collaborative care intervention following on the work of Kilbourne and colleagues (2004). These included:

[20] These are: the collaborative definition of problems; a focus on specific problems; the creation of a range of self-management services; and the provision of active and sustained follow-up.

**Leadership** – by an individual or individuals who can provide continued educational input, engagement with stakeholders, monitor progress and provide feedback, and ensure effective communication. As can be seen from Chapters 7 and 9, this function was largely met, with the possible exception of continued educational input. But this was in the context of the trial and serious consideration would need to be given to how the level of input might be sustained outside of the trial environment or in a larger-scale trial involving a number of primary care centres. The substantial demands on senior staff time in first establishing the conditions to support the trial (many of which centred on the delivery of the interventions and not the details of research design) and then continuing to support the trail throughout its duration would need to be considered in the further development of any collaborative care model. It is likely that the process of discussion of the role of the PCMHW will need continual review; being based in the practices inevitably means that a wide range of factors external to the delivery of collaborative care will impinge on their role. This has implications for the long-term costs effectiveness and potential viability of the model. It is these organisational factors which may go some way to explaining the limited uptake of collaborative care, even in centres closely associated with the original development of the model (for example, Rundall *et al*, 2002)

**Decision support** – including locally tailored protocols for case identification and the delivery of evidence-based interventions linked to referral pathways and systems in order to track progress. In addition, the protocols should be supported by regular training, review of barriers to implementation and systems for routine staff–patient communication. A review of the process evaluation demonstrates that some but not all of these functions were provided. For example, protocols were in place for the delivery of antidepressants and case identification systems (that is, the leaflets, which worked well for those with a previous episode of depression), but systems for tracking progress relied on the limited adaptation of existing systems.

**Clinical information systems** – the chronic care model places considerable emphasis on disease registers (Wagner *et al.*, 2001), which are integrated with existing information systems, including the care planning and monitoring functions of the

service. This links to the issue of decision support above, but no specific register was developed for this trial.

**Delivery system design** – this has two main elements; first, care management (including a direct responsibility for coordinating and providing care and the monitoring of treatment response and adherence); and secondly, the development of "behavioural health linkages" (Kilbourne *et al.*, 2004), which refers to the need to address the frequent comorbidity of depression with chronic physical disorders. Again, the first element was reasonably well met and is discussed in some detail in Chapter 9, but the second element, apart from its appearance in the initial case finding in trial recruitment, was absent.

A particular emphasis in collaborative care interventions has been on supporting compliance with antidepressant medication (Katon *et al.*, 2002 and the meta-regression studies have suggested that this may be associated with positive outcomes. While this trial also aimed to support adherence to medication, and had a protocol for the use of antidepressant medication common to both arms of the trial, there was no indication that the collaborative care intervention improved compliance over and above usual care. Although adherence rates and use of repeat prescriptions compared favourably to other studies, it could be that the lack of prompt contact between the PCMHW and the participants, usually as a result of randomisation and consent procedures, may have resulted in a delay of the supportive intervention, by which time many participants had decided not to take the medication. This has potential implications for the design of future trials including cluster randomisation and revised access to medication support, which are discussed below.

**Psychological interventions**

The position regarding psychological interventions is less clear and two problems need to be addressed. The first concerns the brief interventions and how they were delivered in the study. The effect sizes obtained from the trial were promising and it is possible to speculate that the greater magnitude of the effect size may have arisen from a focus on psychological interventions.(The results of the trial for collaborative care in panic disorder [Roy-Byrne *et al.*, 2005] also support such a view.) However, the low-intensity interventions were quite limited and the long-term effects of such interventions are

uncertain (see Chapter 4). In addition, there was a suggestion from the semi-structured questionnaires that a more extended intervention may be preferred and also that telephone contacts were not as acceptable as face-to-face contacts. This suggests that further refinement of the psychological intervention delivered by the PCMHWs, with more direct contact, could possibly enhance the effectiveness of the intervention.

Secondly, a significant number of people in the trial were referred for a more formal (high-intensity) psychological intervention (41.30% of all trial participants and 37.21% of the collaborative care arm), which was, in nearly all cases, practice-based counselling. Although a review of the impact of this on outcomes did not suggest any significant associations, the precise contribution to the outcome of the trial remains uncertain. If such referrals had little impact on effectiveness they would certainly have had a negative impact on cost. The trial protocol did not limit access to any psychological intervention but these results would suggest that in a future trial consideration should be given to the development of clearer protocols for the use of psychological interventions, perhaps based on some form of stepped-care framework (for example, such as developed in the collaborative care interventions evaluated by Hunkeler *et al.*, 2002 or Bruce *et al.*, 2004)).

### 10.4 The collaborative care model re-visited

The above review of the delivery of the interventions suggests that it is possible to translate the functions of a complex collaborative care intervention from one healthcare setting to another as advocated by Hawe and colleagues (2004). Some deficiencies in delivering all the functions have been noted but in a number of cases they arose as much from issues with the trial design as from a failure to be able to effectively translate the functions for use in another healthcare system. More substantial problems, however, arose from the requirement to make structural and organisational changes to the system for the delivery of care. The extent to which these problems are a failure of replication or a limitation to the collaborative care model itself are discussed below.

#### The chronic disease model

The chronic disease model, as was made clear in Chapter 2, has its origins in the treatment of physical illness (Wagner *et al.*, 1996). This raises the question about the limitations of this model in developing an approach to the treatment of mental illness. A

number of objections to the use of the chronic disease model as a model for the treatment of mental disorders have recently been raised by an anonymous patient with schizophrenia in an article entitled "Why having a mental illness is not like having diabetes" (Anon., 2007). These objections include: the poorer quality treatment received by people with schizophrenia, the stigma associated with mental illness (for patient and family member), the burden felt by family members, the (relatively) unpredictable course of the illness, the impact on the personality, the increased susceptibility to increased external stressors and the loss of privacy (and liberty) that can accompany some treatment interventions. While it could be argued that not all the distinctions between diabetes and schizophrenia (or other mental disorders) may be as clear as the author suggests, these differences potentially do have implications for the application of the collaborative care model to depression. In addition there are other differences between depression and diabetes, which include: the heterogeneous nature of depression, in terms of its course – perhaps for 50% of people it is not a chronic disorder; the differential response of depression to treatment – for some people a complete recovery is possible with effective treatment; its greater responsivity (both positively and negatively to the external environment); and the lack of clear psychological or biological markers (such as the HbA1c measure of glycolated haemoglobin in diabetes), which could reliably indicate the severity of the disease and which may have prognostic value.

A consideration of the above factors suggests a number of developments to the collaborative care model, including a greater consideration of the social and psychological origins and consequences of the disease, including recognition of the stigma associated with mental illness and a greater emphasis on family involvement. These will have implications for the type of interventions offered, including increased range of psychosocial supports, family interventions and explicit attempts to deal with the issues of stigma both at home and in the work place. The very variable course of depression and the limited predictive validity of any diagnostic or related indicators also raise significant questions about the application of collaborative care to all individuals with depression. For many people with self-limiting episodes of depression, the provision of collaborative care (particularly with long-term follow-up over and above that provided by the GP) could be not cost-effective and may be stigmatising. However,

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# Appendices

## Appendix A SSRI Search Filters

### 1. Depression search filter

Data bases - MEDLINE, CINAHL, EMBASE, PsycINFO; All EBM Reviews - Cochrane DSR, ACP Journal Club, DARE, and CCTR.

1. depressive disorder/ or dysthymic disorder/ or seasonal affective disorder/ or depression, involutional/ or depression/

2. depression/ or dysthymia/ or involutional depression/

3. major depression/ or seasonal affective disorder/ or anaclitic depression/ or dysthymic disorder/ or endogenous depression/ or involutional depression/ or reactive depression/ or recurrent depression/ or treatment resistant depression/

4. depression/ or depression, reactive/ or dysthymic disorder/

5. (seasonal affective disorder$ or depress$ or dysthym$).tw. or melancholi$.mp.

6. or/1-5

7. *manic depressive psychosis/

8. *bipolar disorder/

9. *bipolar depression/

10. or/7-8

11. 6 not 10

### 2. Randomised controlled trials search filters

Data bases - MEDLINE, CINAHL, EMBASE, PsycINFO; All EBM Reviews - Cochrane DSR, ACP Journal Club, DARE, and CCTR – OVID interface

*RCTs*

1. exp clinical trials/ or cross-over studies/ or random allocation/ or double-blind method/ or single-blind method/

2. random$.pt.

3. exp clinical trial/ or crossover procedure/ or double blind procedure/ or single blind procedure/ or randomization/

4. exp clinical trials/ or crossover design/ or random assignment/

5. exp clinical trials/ or double blind method/ or random allocation/

6. random$.mp.

7. (cross-over or cross?over or (clinical adj2 trial$) or single-blind$ or single?blind$ or double-blind or double?blind$ or triple-blind or triple?blind).tw.

8. or/1-7

9. animals/ not (animals/ and human$.mp.)

10. animal$/ not (animal$/ and human$/)

11. meta-analysis/

12. meta-analysis.pt.

13. systematic review/

14. or/9-13

15. 8 not 14

*SSRIs v placebo*

Data bases - MEDLINE, CINAHL, EMBASE, Cochrane Controlled Trials Register, PsycINFO, CINAHL

1. citalopram/ or fluoxetine/ or paroxetine/ or sertraline hydrochloride/

2. sertraline/ or fluvoxamine/

3. (Citalopram or akarin or celexa or cipram or cipramil or elopram or prisdal or sepram or seralgan or seropram or talohexal).tw

4. (Fluoxetine or adofen or afeksin or affectine or affex or astrin or atd or auscap or daforin or deprax or deprexin or deproxin or diesan or digassim or docutrix or erocap or eufor or felicium or fluctin or fluctine or flumed or fluneurin or fluocim or fluohexal or fluox or fluoxac or fluoxemerck or fluoxeren or flouxibene or fluoxifar or fluoxine or fluox-puren or flusol or flutin or flutine or flux or fluxantin or fluxene or fluxet or fluxetil or fluxetin or fluxac or fondur or fontex or fonzac or geroxac or lorien or lovan or magrilan or motvone or mutan or nodepe or norzac or nuzak or nyucoflox or oxetine or oxsac or plinzene or positivum or prizma or prodep or provatine or prozac or prozamel or prozatan or prozyn or psipax or reneuron or salipax or sanzur or sarafem or seromex or seronil or seroscand or siquial or tuneluz or verotina or zactin).tw

5. (Fluvoxamine or desifluvoxamin or dumirox or dumyrox or faverin or favoxil or floxyfral or fluvoxadura or luvox or maveral).tw

6. (Paroxetine or aropax or casbol or deroxat or frosinor or motivan or paxetil or paxil or sereupin or seroxat or tagonis).tw

7. (Sertraline or lustral or altruline or aremis or besitran or gladem or sealdin or tatig or tresleen or Zoloft or altruline or serad or serlain).tw

8. or/1-8

## Appendix B Methodological Quality Check

| | | |
|---|---|---|
| *Quality checklist for an RCT* | | |
| **Report reference ID:** | | |
| **Checklist completed by:** | | **Date completed:** |
| ***SECTION 1: INTERNAL VALIDITY*** | | |
| **Evaluation criteria** | | **How well is this criterion addressed?** |
| **1.1** | **Was the assignment of subjects to treatment groups randomised?** | |
| ***If there is no indication of randomisation, the study should be rejected.*** *If the description of randomisation is poor, or the process used is not truly random (e.g., allocation by date, alternating between one group and another) or can otherwise be seen as flawed, the study should be given a lower quality rating.* | | |
| **1.2** | **Was an adequate concealment method used?** | |
| *Centralised allocation, computerised allocation systems, or the use of coded identical containers would all be regarded as adequate methods of concealment, and may be taken as indicators of a well-conducted study. If the method of concealment used is regarded as poor, or relatively easy to subvert, the study must be given a lower quality rating, and can be rejected if the concealment method is seen as inadequate.* | | |
| ***SECTION 2: OVERALL ASSESSMENT*** | | **Comments** |
| 2.1 | Low risk of bias | **Both criteria met** |
| | Moderate risk of bias | *One or more criteria partly met* |
| | High risk of bias | *One or more criteria not met* |

| **Area:** | | | **Report reference ID:** | | |
|---|---|---|---|---|---|
| **Comparisons:** | | | | | |
| Ref List checked | | Data entered in Rev Man | | Characteristics entered | |
| Data Checked | | Reference Manager updated | | Excluded | |
| **Randomised?** | | | **Blind?** | | |
| Setting: | | In/Out/Mixed/Primary Care (80% patients) | | | |
| Analysis: | | Completer/ITT (continuous data) | | | |
| Diagnosis | | | % Dysthymic | | |
| | | | % Bipolar | | |
| Mean baseline | | | | | |
| Trial length | | | | | |
| Interventions (Dose):<br>1<br>2<br>3 | | | | | |
| Notes | | | | | |

## Appendix C American Psychiatric Association Severity Criteria

**The Hamilton Rating Scale for Depression (HRSD)**
The HRSD is a 21-item clinician-completed scale, although usually only the first 17 items are scored. There is also a 24-item version.

The items covered are depressed mood, guilt feelings, suicide, insomnia –early, insomnia – middle, insomnia – late, work and activities, retardation – psychomotor, agitation, anxiety – psychological, anxiety – somatic, somatic symptoms GI, somatic symptoms – general, sexual dysfunction – menstrual disturbance, hypochondrias, weight loss – by history and by scales, insight.

The additional items in the 21-item version are diurnal variation, depersonalisation and derealisation, paranoid symptoms, and obsessional and compulsive symptoms.

Since it was developed before RDC or DSM-III criteria for depression, it does not include symptoms that are part of these definitions, such as anhedonia (APA, 2000). It gives more weight to somatic symptoms than to cognitive ones (APA, 2000).

***Scoring and levels of depression***
Items are scored 0-4 or 0-2, giving a total score range of 0-50 on the 17-item version.

**Cut-offs for levels of depression severity on the HRSD adopted by various authorities**

| | *Not depressed* | *Mild* | *Moderate* | *Severe* | *Very severe* |
|---|---|---|---|---|---|
| HRSD-website | | 10-13 | 14-17 | >17 | |
| Elkin *et al*, 1989 | <= 6 | 10-20 | 20-30 | >30 | |
| Keller *et al*, 2000 | <=8 | | | | |
| APA 2000a | 0-7 | 8-13 | 14-18 | 19-22 | >23 |

The APA criteria were adopted for the analyses in this thesis.

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Elkin, I., Shea, M.T., Watkins, J.T., *et al.* (1989) National Institute of Mental Health Treatment of Depression Collaborative Research Program. General effectiveness of treatments. *Archives of General Psychiatry*, *46*, 971-982.

HRSD website – http://www.rag.org.au/drbill/depresstest.htm

Keller, M. B., McCullough, J. P., Klein, D. N., *et al.* (2000) A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. *New England Journal of Medicine*, *342*, 1462-1470.

## Appendix D Data Extraction Form

| Completed by: | | | | | | Report reference ID: | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *1 TREATMENT GROUP:* | | | | | | | | | | | |
| **Dropouts** | | **Treatment Responders** | | **Side Effects (total)** | | | | | | | |
| *n* | *N* | *n* | *N* | *n* | *N* | *n* | *N* | | | | |
| | | | | | | | | | | | |
| **Definition of responders** | | | | | | | | | | | |
| **Post-treatment means** | | | | | | | | | | | |
| *n* | *Mean* | *SD* | *n* | *Mean* | *SD* | *n* | *Mean* | *SD* | *n* | *Mean* | *SD* |
| | | | | | | | | | | | |
| **Other data** | | | | | | | | | | | |
| *n* | *N* | *n* | *N* | *n* | *Mean* | *SD* | *n* | *Mean* | *SD* | | |
| | | | | | | | | | | | |
| *2 TREATMENT GROUP:* | | | | | | | | | | | |
| **Dropouts** | | **Treatment Responders** | | **Side Effects (total)** | | | | | | | |
| *n* | *N* | *n* | *N* | *n* | *N* | *n* | *N* | | | | |
| | | | | | | | | | | | |
| **Definition of responders** | | | | | | | | | | | |
| **Post-treatment means** | | | | | | | | | | | |
| *n* | *Mean* | *SD* | *n* | *Mean* | *SD* | *n* | *Mean* | *SD* | *n* | *Mean* | *SD* |
| | | | | | | | | | | | |
| **Other data** | | | | | | | | | | | |
| *n* | *N* | *n* | *N* | *n* | *Mean* | *SD* | *n* | *Mean* | *SD* | | |
| | | | | | | | | | | | |

## Appendix E Conversion Formulae

The following formulae were used to calculate standard deviations (SD) where these were not available in study reports:

(n = sample size of group)

$$SD = \text{Standard Error} \times \sqrt{n}$$

$$SD = \frac{(\text{upper 95\% Confidence Interval} - \text{mean})}{1.96} \times \sqrt{n}$$

$$SD = \frac{(\text{mean}_1 - \text{mean}_2)}{\sqrt{F}\,(\sqrt{1/n_1} + \sqrt{1/n_2})}$$

(If F ratio is not given, then $F = t_2$)

## Appendix F Included and Excluded Studies – SSRIs

### *References to included studies*

* indicates the primary reference for the study

**ANDREOLI2002** {published data only}

* Andreoli V, Caillard V, Deo RS, Rybakowski JK, Versiani M. Reboxetine, a new noradrenaline selective antidepressant, is at least as effective as fluoxetine in the treatment of depression. Journal of Clinical Psychopharmacology 2002;22(4):393-399.

Dubini A. Do noradrenaline and serotonin differentially affect social motivation and behaviour? European Neuropsychopharmacology Vol 7 Suppl 1, pp S49-55; discussion S71-3, 1997.

Dubini A. Noradrenaline-selective versus serotonin-selective antidepressant therapy: differential effects on social functioning. Journal of Psychopharmacology 11(4 Suppl):S17-23, 1997.

Healy D. Reboxetine: its effects as measured by the Social Adaptation Self-evaluation Scale. [Review] [36 refs]. Acta Psychiatrica Scandinavica, Supplementum 2000;402:45-51.

**BURKE02** {published and unpublished data}

* Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. Journal of Clinical Psychiatry 2002;63(4):331-336.

Owens MJ, Rosenbaum JF. Escitalopram: A second-generation SSRI. Cns Spectrums 2002;7(4 SUPPL. 1):34-39.

**BYERLEY88** {published data only}

Byerley WF, Reimherr FW, Wood DR, Grosser BI. Fluoxetine, a selective serotonin uptake inhibitor, for the treatment of outpatients with major depression. J Clin Psychopharmacol 1988;8:112-5.

**CLAGHORN1996** {published data only}

Claghorn JL, Earl CQ, Walczak DD, Stoner KA, Wong LF, Kanter D, Houser VP. Fluvoxamine maleate in the treatment of depression: a single-center, double-blind, placebo-controlled comparison with imipramine in outpatients. Journal of Clinical Psychopharmacology 1996;16(2):113-120.

**CLAGHORN92A** {published data only}

Claghorn J. A double-blind comparison of paroxetine and placebo in the treatment of depressed outpatients. International Clinical Psychopharmacology Vol 6 Suppl 4, pp 25-30, 1992.

* Claghorn JL. The safety and efficacy of paroxetine compared with placebo in a double-blind trial of depressed outpatients. Journal of Clinical Psychiatry 1992;53 Suppl:33-35.

**COHN1985** {published data only}

Cohn,J.B.; Wilcox,C.. A comparison of fluoxetine, imipramine and placebo in pateints with major depressive disorders. Clinical Psychiatry 1985;46:26-31.

**COLEMAN01** {published data only}

Coleman CC, King BR, Bolden-Watson C, Book MJ, Segraves RT, Richard N, Ascher J, Batey S, Jamerson B, Metz A. A placebo-controlled comparison of the effects on sexual functioning of bupropion sustained release and fluoxetine. Clinical Therapeutics 2001;23(7):1040-1058.

**COLEMAN1999**{published data only}

Coleman CC, Cunningham LA, Foster VJ, Batey SR, Donahue RM, Houser TL, Ascher JA. Sexual dysfunction associated with the treatment of depression: a placebo-controlled comparison of bupropion sustained release and sertraline treatment. Annals of Clinical Psychiatry 1999;11(4):205-215.

**CONTI1988** {published data only}

Conti L. Fluvoxamine maleate: Double-blind clinical trial vs placebo in hospitalized depressed patients. Current Therapeutic Research, Clinical & Experimental 43(3):468-480, 1988.

**CROFT1999** {published data only}

* Croft H. A placebo-controlled comparison of the antidepressant efficacy and effects on sexual functioning of sustained-release bupropion and sertraline. Clinical Therapeutics 21(4):643-58, 1999.

Croft HA AJBSH. A comparison of bupropion SR, sertraline and placebo in depressed outpatients. 152nd Annual Meeting of the American Psychiatric Association Washington DC, USA 15-20th May, 1999.

**DOMINGUEZ85** {published data only}

Dominguez RA, Goldstein BJ, Jacobsen AF, Steinbook RM. A double blind controlled study of fluvoxamine and imipramine in depression. J Clin Psychiatry 1985;46:84-7.

**DUNLOP1990** {published data only}

Dunlop SR, Dornseif BE, Wernicke JF, Potvin JH. Pattern analysis shows beneficial effect of fluoxetine treatment in mild depression. Psychopharmacology Bulletin 1990;26(2):173-180.

**EDWARDS93** {published data only}

Edwards JG, Goldie A. Placebo-controlled trial of paroxetine in depressive illness. Human Psychopharmacology 1993;8(3):203-209.

**FABRE1996** {published data only}

* Fabre L, Birkhimer LJ, Zaborny BA, Wong LF, Kapik BM. Fluvoxamine versus imipramine and placebo: a double-blind comparison in depressed patients. International Clinical Psychopharmacology 1996;11(2):119-127.

Fabre L. Fluvoxamine in the treatment of depression - A double-blind comparison with imipramine and placebo in outpatients with major depression. Clinical Neuropharmacology 15(Suppl 1, Pt B):416B, 1992.

**FABRE95** {published data only}

Fabre LF, Abuzzahab FS, Amin M, Claghorn JL, Mendels J, Petrie WM, Dube S, Small JG. Sertraline safety and efficacy in major depression: a double-blind fixed-dose comparison with placebo. Biological Psychiatry 1-11-1995;38(9):592-602.

**FEIGHNER1989** {published data only}

Feighner JP, Boyer WF, Meredith CH, Hendrickson GG. A placebo-controlled inpatient comparison of fluvoxamine maleate and imipramine in major depression. International Clinical Psychopharmacology 1989;4:239-244.

**FEIGHNER99** {published data only}

Bech P, Tanghoj P, Andersen HF, Overo K. Citalopram dose-response revisited using an alternative psychometric approach to evaluate clinical effects of four fixed citalopram doses compared to placebo in patients with major depression. Psychopharmacology 2002;163(1):20-25.

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Feighner JP, Overo K. Multicenter, placebo-controlled, fixed-dose study of citalopram in moderate-to-severe depression. Journal of Clinical Psychiatry 1999;60(12):824-830.

**FEIGHNER89A** {published data only}

Feighner JP, Boyer WF, Merideth CH, Hendrickson GG. A double-blind comparison of fluoxetine, imipramine and placebo in outpatients with major depression. International Clinical Psychopharmacology 1989 Apr;4(2):127-34.

**FEIGHNER92** {published data only}

Cohn JB WC. Paroxetine in major depression: a double-blind trial with imipramine and placebo. Journal of Clinical Psychiatry Vol 53 Suppl, pp 52-6, 1992.

Cohn JB, Crowder JE, Wilcox CS, Ryan PJ. A placebo- and imipramine-controlled study of paroxetine. Psychopharmacology Bulletin 1990;26:185-189.

Dunbar GC, Cohn JB, Fabre LF, Feighner JP, Fieve RR, Mendels J, Shrivastava-RK AA, imipramine-and-placebo-in-depressed-out-patients. A comparison of paroxetine, imipramine and placebo in depressed out-patients. British Journal of Psychiatry 1991;159:394-398.

Fabre LF. A 6-week, double-blind trial of paroxetine, imipramine, and placebo in depressed outpatients. Journal of Clinical Psychiatry Vol 53 Suppl, pp 40-3, 1992.

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Itil TM, Shrivastava RK, Mukherjee S, Coleman BS, Michael ST. A double blind placebo-controlled study of fluvoxamine and imipramine in out patient s with primary depression. Br J Clin Pharmacol 1983;15:433-8s.

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Amin MM, Anath JV, Coleman BS, Darcourt G, Farkas T, Godlstein BB. Fluvoxamine; antidepressant effects confirmed in a placebo controlled international study. 1984;7:580-581.

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Agosti V, McGrath PJ. Comparison of the effects of fluoxetine, imipramine and placebo on personality in atypical depression. Journal of Affective Disorders 2002;71(1-3):113-120.

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**MONTGOMERY2001** {published data only}

Montgomery SA, Loft H, Sanchez C, Reines EH, Papp M. Escitalopram (S-enantiomer of citalopram): clinical efficacy and onset of action predicted from a rat model. Pharmacology & Toxicology 2001;88(5):282-286.

**MONTGOMERY92A** {published data only}

Montgomery SA, Rasmussen JG, Lyby K, Connor P. Dose response relationship of citalopram 20 mg, citalopram 40 mg and placebo in the treatment of moderate and severe depression. International Clinical Psychopharmacology 1992;6(Suppl 5):65-70.

**NORTON1984** {published data only}

Norton KRW, Sireling LI, Bhat AV, Rao B, Paykel ES. A double blind comparison of fluvoxamine, imipramine and placebo in depressed patients. J Affect Disord 1984;7:297-308.

**O'FLYNN1991** {published data only}

O'Flynn K. Effect of fluoxetine on noradrenergic mediated growth hormone release: a double blind, placebo-controlled study. Biological Psychiatry 30(4):377-82, 15-8-1991.

**RAVINDRAM 1995** {published data only}

Ravindram AV, Teehan MD, Bakish D, Yatham L, O-Reilly R, Fernando ML, Manchanda R, Charbonneau Y, Buttars J. The impact of sertraline, desipramine, and placebo on psychomotor functioning in depression. HUM PSYCHOPHARMACOL 1995;10(4):273-281.

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Reimherr FW, Chouinard G, Cohn CK, Cole JO, Itil TM, LaPierre YD, Masco HL - Mendels J. Antidepressant efficacy of sertraline: a double-blind, placebo- and amitriptyline-controlled, multicenter comparison study in outpatients with major depression [see comments]. Journal of Clinical Psychiatry 1990 Dec;51 Suppl B:18-27.

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**RICKELS1992** {published data only}

Rickels K. The efficacy and safety of paroxetine compared with placebo in outpatients with major depression. Journal of Clinical Psychiatry Vol 53 Suppl, pp 30-2, 1992.

**ROTH90** {published data only}

Roth D, Mattes J, Sheehan KH, Sheehan DV. A double-blind comparison of fluvoxamine, desipramine and placebo in outpatients with depression. Progress in Neuro-Psychopharmacology & Biological Psychiatry 1990;14(6):929-39.

**RUDOLPH99** {published data only}

Entsuah R, Gorman JM. Global benefit-risk assessment of antidepressants: venlafaxine XR and fluoxetine. Journal of Psychiatric Research 2002;36(3):111-118.

Rudolph RL, Feiger AD. A double-blind, randomized, placebo-controlled trial of once-daily venlafaxine extended release (XR) and fluoxetine for the treatment of depression. Journal of Affective Disorders 1999;56(2-3):171-181.

**SIL'STNE99** {published and unpublished data}

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## Appendix G Characteristics of Included Studies – SSRIs

**Notes on the use of the Tables**

**Version of The HRSD used** - H*nn* refers to the version of the HRSD used in the efficacy analysis, i.e. = HRSD-21.

**Methods** - describes the design of the trial including details of randomisation and blinding, the duration of the trial and whether analysis of continuous data was carried out on an intention-to-treat or completer sample. In some cases intention-to-treat may not refer to the number of patients originally randomised to each treatment group since many studies defined their own criteria, commonly that patients included in the intention-to-treat sample must have received at least one dose of study drug, and undergone at least one assessment.

**Participants** - details of the patients who entered trials and the criteria for their inclusion in the study, patient setting, number of patients randomised, age range or mean age, number of female participants, diagnostic inclusion criteria and baseline depression scale scores, country in which the trial took place. This information refers to the total number of patients randomised in a study; where there were more than two treatment groups it may not relate to the patients entered into the review.

**Interventions** - lists all the treatment groups that patients could be assigned to; in pharmacological trials the dose range or mean dose administered to patients is given. In trials with more than two treatment arms a note is made of which groups were used in the review.

**Doses of pharmacological treatments** are indicated as follows:

*nn*mg->*nn*mg indicates that all patients started on *nn*mg and increased to *nn*mg

*nn*mg up to *nn*mg means that all patients initially received *nn*mg and this was increased to a maximum of *nn*mg for some patients (usually those who did not respond to the lower dose or those who could tolerate an increase)

*nn-nn* mg means that patients received between *nn*mg and *nn*mg.

**Outcomes** - lists the outcomes that have been extracted including how 'response' and 'remission' have been defined by individual studies where appropriate.

**Notes** - contains additional information, for example, where the study was carried out and by whom, and mean baseline depression scale scores.

**Allocation concealment (AC)** - grades studies from A-D according to how well treatment group assignment was concealed from investigators and patients. 'A' indicates concealment was adequate, 'B' unclear, 'C' inadequate, and 'D' indicates that allocation concealment was not used as a criterion to assess validity.

## The following abbreviations are used in the tables:

| | | |
|---|---|---|
| BDI = Beck Depression Inventory | GHQ = General Health Questionnaire | MADRS = Montgomery-Asberg Depression Rating Scale |
| CGI = Clinical Global Impressions | HRSD = Hamilton Rating Scale for Depression | RDC = Research Diagnostic Criteria |
| CIS = Clinical Interview Schedule | ITT = intention-to-treat | SADS = Schedule for Affective Disorders and Schizophrenia |
| DSM = Diagnostic Statistical Manual | LOCF = last observation carried forward | SE = standard error |

## Characteristics of included studies

| Study | Methods | Participants | Interventions | Outcomes | Notes | AC |
|---|---|---|---|---|---|---|
| Andreoli 2002 | Allocation: Random (no details). Duration: 8 weeks (+4 to 28-day washout). Analysis: ITT. | Inpatients and outpatients. N=381. Age: 18-65. Diagnosis: DSM-III-R major depression without psychotic features, HRSD≥22. | 1. Reboxetine (8mg up to 10mg after 4 weeks). 2. Fluoxetine (20mg up to 40mg after 4 weeks). 3. Placebo. | 1. Non-responders (patients not achieving ≥50% decrease in HRSD). 2. Non-remitters (patients not achieving HRSD≤10). 3. Leaving the study early. 4. Leaving the study early due to side effects. 5. Patients reporting side effects. | Conducted in 33 centres in 6 countries. | B |
| Burke02 | Allocation: Random no details. Duration: 8 weeks (+ 1 week placebo washout). Analysis: LOCF. | Outpatients. N=491. Age: 18-65. Diagnosis: DSM-IV major depressive disorder, MADRS ≥22 Baseline scores: Escitalopram 10mg - MADRS=28.0+-4.9, HRSD-24=24.3+-6.2. Escitalopram 20mg - MADRS=28.9+-4.6, HRSD- | 1. Escitalopram (10mg). 2. Escitalopram (20mg). 3. Citalopram (40mg). 4. Placebo. (1 and 2 not extracted) | 1. HRSD-24 mean change scores. 2. Non-responders (patients not achieving ≥50% decrease in HRSD). 3. Leaving the study early. 4. Leaving the study early due to side effects. 5. Patients reporting side effects. | Conducted at 35 centres in the US. | B |

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| | | 24=25.8+-5.7 Citalopram - MADRS=29.2+-4.5, HRSD-24=25.9+-5.9. Placebo - MADRS=29.5+-5.0, HRSD-24=25.8+-5.9. | | | | |
| Byerley 88 | Double blind RCT Concealment of Allocation: Unclear. Analysis: Completer. Active Treatment: 6 weeks. | Inclusion criteria: DSM-III-R major depression of at least 1 month 20+ HRSD (21). Mean age: 39. N=97, HRSD analysis: N=60. Country: US Setting: Outpatients | Fluoxetine versus imipramine (75mg -> 150mg by day 15) versus placebo. | 1. HRSD-21mean endpoint scores. 2. Leaving the study early. 3. Leaving the study early due to side effects. | | B |
| Claghorn 1996 | Double-blind RCT Concealment of Allocation: Unclear. Analysis: Completer. Active treatment: 6 weeks. | Inclusion criteria: DSM-III major depression. Age: 39 (+-10.9) years; N=150, HRSD analysis: N=61. Country: America. Setting: Outpatient. | 1. Fluvoxamine (mean dose during 4th week 128.5 mg). 2. Imipramine (mean dose during fourth week 186.8 mg). 3. Placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | | B |
| Claghorn 92 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: not clear, but irrelevant as efficacy data not extractable. Active treatment: 6 weeks. | Inclusion criteria: DSM-III major depression, 18+ on HRSD-21; mean baseline HRSD: Paroxetine group 25 (+-0.59); Placebo group 24.6 (+-0.65). N=72 (71 in efficacy sample); 23 female. Mean age: approximately 35 (18-65). Country: US. Setting: Outpatient. | Paroxetine (mean 28.3 mg) versus placebo | 1.HRSD mean endpoint scores. * 2. Non-responders (patients not achieving ≥50% reduction in HRSD). 3. Leaving the study early. 4. Leaving the study early due to side effects. | * from Claghorn1992 | B |
| Cohn 1985 | Allocation: Random (no details). | Outpatients. N=166; 98 female. Age: 20- | 1. Fluoxetine. (20-80mg) 2. Placebo | 1. Leaving the study early. 2. Leaving the | Same protocol as Stark 1985 but different | B |

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| | Duration: 6 weeks (+1 week washout). Analysis: ITT. | 64. Diagnosis: DSM-III major depressive illness, HRSD≥20. | 3. Imipramine | study early due to side effects. | patients. | |
| Coleman 01 | Allocation: Random (no details). Duration: 8 weeks (+1 week washout). Analysis: ITT (≥1 assessment post-baseline). | Outpatients. N=456 (HRSD analysis: N=427). Age: 18-76, mean=36.6-37.1. Diagnosis: DSM-IV moderate-severe recurrent major depression, HRSD-21≥20. Mean baseline HRSD: Placebo - 24.4, fluoxetine - 24.5 (ITT sample). | 1. Fluoxetine (20-60mg, mean = 26mg). 2. Placebo. 3. Bupropion SR. | 1.Leaving the study early. 2. Leaving the study early due to side effects. | Extracted data for 1 and 2 only. | B |
| Coleman 1999 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: ITT (≥1 dose of medication and ≥1 post-baseline assessment). Active treatment: 8 weeks. | Inclusion criteria: DSM-IV recurrent moderate to severe depression, 18+ on HRSD-31; mean baseline HRSD: 34; all in stable relationship (sexual function was focus of study). Age: 18-74; mean 38 years. N=242 (without buproprion group). Country: US. Setting: Classified as 'mixed' as not clear. | Sertraline versus placebo (versus buproprion - not extracted) (sertraline: mean 106 mg/day) | 1. Non-responders (patients not achieving ≥50% reduction in HRSD). 2. Leaving the study early. 3. Leaving the study early due to side effects. | Undertaken in 11 centres. | B |
| Conti 1988 | Allocation: Random (no details). Duration: 4 weeks (+3-7 day washout). | Inpatients. N=45, all female. Age: 18+, mean=53. Diagnosis: DSM-III major depressive episode, HRSD≥16. | 1. Fluvoxamine (50-300mg, mean=273mg). 2. Placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | Originally part of Amin 1984 multi-centre trial, but not included in that data and published separately. | B |
| Croft 1999 | Double blind RCT | Inclusion criteria: DSM- | Sertraline versus placebo (versus | 1. Non-responders | Undertaken in eight centres. | B |

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| | Concealment of Allocation: Unclear. Analysis: ITT (≥1 dose of medication and ≥1 post-baseline assessment). Active treatment: 8 weeks. | IV moderate to severe depression, 18+ on HRSD-31; mean baseline HRSD: 32.78; all in stable relationship (sexual function was focus of study). Age: 19-30. N=360, HRSD analysis: N=348 Country: US. Setting: Classified as 'mixed' as not clear. | buproprion - not extracted) (sertraline: mean 121 mg/day) | (patients not achieving ≥50% reduction in HRSD). 2. Leaving the study early. 3. Leaving the study early due to side effects. | | |
| Doming-uez85 | Double-blind RCT Concealment of Allocation: Unclear. Analysis: ITT. Active treatment: 4 weeks. | Inclusion criteria: DSM-III major depression. N=101. Age: 21-64 years. Country: US. Setting: Outpatient. | 1. Fluvoxamine (100-300mg). 2. Imipramine. 3. Placebo. | 1. Leaving the study early. | Leaving study early due to side effects and mean endpoint data included in Kasper 1995. | B |
| Dunlop 1990 | Allocation: Random (no details). Duration: 6 weeks. Analysis: ITT. | Outpatients. N=372; 58% female. Age: 19-70, mean=39.3. DSM-III major depressive disorder, HRSD≥14 and ≤19. Raskin > Covi anxiety score. | 1. Fluoxetine (20mg). 2. Fluoxetine (40mg). 3. Fluoxetine (60mg). 4. Placebo. | 1. HRSD mean change scores (20mg only). 2. Non-responders (patients not achieving ≥50% decrease in HRSD). 3. Leaving the study early. 4. Leaving the study early due to side effects. | Dichotomous data is combined for 20, 40 and 60mg groups. | B |
| Edwards 93 | Allocation: Random (no details). Duration: 6 weeks. Analysis: ITT. | Outpatients. N=41; 23 female. Age: 18-65, mean=44. Diagnosis: DSM-III major depression (all but three patients met the criteria) or Feighner criteria definite depression (all but three met this criteria), | 1. Paroxetine (30mg). 2. Placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | | B |

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| | | HRSD-17≥18. | | | | |
| Fabre 1996 | Allocation: Random (no details). Duration: 6 weeks (+ 7-14 day placebo washout). Analysis: ITT (≥1 dose & ≥1 post-baseline assessment). | Outpatients. N=150. Age: 18-65. Diagnosis: DSM-III major depressive disorder, HRSD-21≥20, Raskin depression ≥8 and > Covi anxiety score. | 1. Fluvoxamine (mean at week 6 =117mg). 2. Placebo. 3. Imipramine. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | | B |
| Fabre95 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: ITT (≥1 dose of medication and ≥1 post-baseline assessment). Active treatment: 6 weeks. | Inclusion criteria: DSM-III for major depressive episode (2% bipolar), 22+ on HRSD-17; mean baseline HRSD: 24.8 to 25.7. Age: mean 37. 149 female. N=277, HRSD analysis: N=258. Country: US. Setting: Classified as 'mixed' as not clear. | Sertraline (three groups) versus placebo (Group 1: mean 50mg [not extracted]; Group 2: mean 98mg; Group 3: mean 190 mg).* Dichotomous outcomes: Groups 2 and 3 added. Continuous outcomes: Group 2 only. | 1. Leaving the study early. 2. Leaving the study early due to side effects. 3. Patients reporting side effects. | * overall mean dose for 100mg + 200mg groups is 144mg | B |
| Feighner 1989 | Allocation: Random (no details). Duration: 6 weeks (+3 day placebo washout). Analysis: ITT. | In-patients Age: 18-71, mean=41. Diagnosis: major depression | 1. Fluvoxamine (150-300mg, mean=145mg). 2. Placebo. 3. Imipramine. | 1. Leaving the study early due to side effects. | | B |
| Feighner 99 | Allocation: Random no details. Duration: 6 weeks (+ 1week placebo washout). Analysis: LOCF. | Outpatients. N=650. Age: 18-65. Diagnosis: DSM-III-R major depression, HRSD-21≥20. Baseline scores: All Citalopram - MADRS=27.5, HRSD-21=24.6 Placebo - MADRS=27.1, HRSD-21=24.6. | 1. Citalopram (10mg). 2. Citalopram (20mg). 3. Citalopram (40mg). 4. Citalopram (60mg). 5. Placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | | B |
| Feighner 89 | Double Blind RCT Concealment of Allocation: | Inclusion criteria: DSM-III major depression, 20+ | Fluoxetine versus imipramine (72% achieved | 1. Leaving the study early. 2. Leaving the study early due | | B |

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| | Unclear. Analysis: ITT (≥2 weeks treatment). Active treatment: 6 weeks. | HRSD (21), 8+ on Raskin scale, and greater than Covi scale. Age: 18-70. N=179, HRSD analysis: N=145. Country: US. Setting: Outpatients. | >150mg) versus placebo. | to side effects. | | |
| Feighner 92 | Random (no details). Duration: 6 weeks. Analysis: ITT (> 1 post baseline efficacy). | Outpatients. N=726. Age: 18-65, mean=40. Diagnosis: DSM-III major depressive episode, HRSD-17≥18. Raskin depression> Covi anxiety score. Mean Baseline HRSD: Paroxetine - 26.4, placebo - 26.6. | 1. Paroxetine (10-20mg, mean = 28.7-45.5mg). 2. Placebo. 3. Imipramine. | 1. Leaving the study early. 2. Leaving the study early due to side effects. 3. Patients reporting side effects. | | B |
| Hackett 96 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: ITT. Active Treatment: 8 weeks. | Inclusion criteria: DSM-III-R major depression, HRSD-21≥20. Age: 18+. Country: Europe. Setting: Outpatients. Mean baseline HRSD=26.6. | Paroxetine versus venlafaxine (150mg). | HRSD-21 mean endpoint scores. | | B |
| Itil 1983 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: Completer. Active Treatment: 4 weeks. | Inclusion criteria: RDC major affective disorder. Age: 21-68. N=69, HRSD analysis: N=37. Country: US. Setting: Outpatients. | Fluvoxamine versus imipramine (50mg -> 150mg on day 3, up to 300mg on day 8, mean=127mg +/- 46mg) versus placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | 4% patients diagnosed with bipolar disorder. | B |
| Kasper95 | Double-blind RCT Concealment of Allocation: Unclear. Analysis: Completer. Active treatment: 4 weeks. | Inclusion criteria: DSM-III major depression or DSM-III bipolar disorder (14%). Age: 42.3 years; N=338, HRSD analysis: N=313. Country: Canada | 3-7 day washout; inpatients received study medication for at least 2 weeks in hospital; after gradually increasing dose during first 3 | 1. HRSD-16 mean endpoint scores (17 item scale, but "loss of weight" item not included because of difficulties in interpreting changes in body | Paper reports on five N. American centres in Amin 1984 (no extractable data) which includes Dominguez 1985 and Lapierre 1987. | B |

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| | | and America. Setting: Mixed. | days, dose range 50-300mg/day t.i.d. Fluvoxamine: Mean dose 158.5 mg. Imipramine: Mean dose 151 mg (data not extracted). Placebo. | weight, so only 16 items used). 2. Leaving the study early due to side effects. | Therefore the data here includes patients from those studies along with the remaining three centres. | |
| Lapierre 1987 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: Completer. Active Treatment: 6 weeks. | Inclusion criteria: DSM-III-R major depressive disorder, 15+ HRSD. Age: 20-69. N=63, HRSD analysis: N=10. Country: Canada. Setting: Inpatients. | 1. Fluvoxamine (50-300mg, mean=180.3mg). 2. Imipramine. 3. Placebo. | 1. Leaving the study early. | Leaving study early due to side effects and mean endpoint data included in Kasper 1995. | B |
| Lydiard 1989 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: Completer. Active Treatment: 6 weeks. | Inclusion criteria: DSM-III-R major depression, 22+ HRSD. Age: 18+. N=54, HRSD analysis: N=52. Country: US. Setting: Outpatients. | 1. Fluvoxamine (100-300mg, mode=240+-60mg). 2. Imipramine. 3. Placebo. | 1. Non-responders (patients not achieving ≥50% decrease in HRSD and at least "much improved" on CGI). 2. Leaving the study early due to side effects. | | B |
| McGrath 00 | Allocation: Random (no details). Duration: 10 weeks. Analysis: ITT-LOCF. | Setting: unclear. N=154. Age: 18-65, mean=41.6. Diagnosis: DSM-IV major depressive episode and Columbia criteria for atypical depression. | Fluoxetine (mean=51.4+-14.6mg) versus imipramine (50mg->300mg, mean=204.9+-90.7mg) versus placebo. | 1. HRSD-17 mean endpoint scores. | | B |
| Mendels 1999 | Allocation: Random no details. Duration: 4 weeks (+ 1week placebo washout). Analysis: LOCF | Outpatients. N=180. Mean age: 43. Diagnosis: DSM-III melancholia plus DSM-III major depression or bipolar, depressed‡. | 1. Citalopram (20mg up to 80mg). 2. Placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | ‡ only 9/180 (5%) patients were diagnosed bipolar (depressed). Conducted at 3 centres in the US. | B |

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| | | HRSD-24≥25. Baseline scores: Citalopram - HRSD-17=23.9+-3.2. Placebo - HRSD-17=24.1+-3.5 | | | | |
| Miller 1989 | Double Blind RCT Concealment of Allocation: unclear. Analysis: not clear, but irrelevant as efficacy data not extractable. Active treatment: 4 weeks. | Inclusion criteria: Feighner criteria for depression, 18+ on HRSD-21; mean baseline HRSD: paroxetine group 22.7; placebo group 24.2. N=47; 32 female. Mean age: 42. Country: UK. Setting: Outpatient. | Paroxetine (mean 30 mg) versus placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | | B |
| Montgo-mery 01 | Allocation: Random no details. Duration: 8 weeks (+ 1week placebo washout). Analysis: LOCF. | Primary care patients. N=471. Mean age: 43 +- 11. Diagnosis: DSM-IV major depressive disorder, MADRS ≥22 & ≤40. Baseline scores: Escitalopram - MADRS=29 Citalopram - MADRS=29.2 Placebo - MADRS=28.7. | 1. Escitalopram (10mg up to 20mg). 2. Citalopram (20mg up to 40mg). 3. Placebo. (1 not extracted) | 1. Leaving the study early. 2. Leaving the study early due to side effects. 3. Patients reporting side effects. | Conducted at 69 primary care centres in Europe. | B |
| Montgo-mery 92 | Allocation: Random no details. Duration: 6 weeks (+ 1week placebo washout). Analysis: LOCF. | Inpatients and outpatients. N=199; 138 female. Age: 19-72, mean 44. Diagnosis: DSM-III-R major depression, MADRS≥22. | 1. Citalopram (20mg). 2. Citalopram (40mg). 3. Placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | Conducted in the UK. | B |
| Norton 1984 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: ITT. | Inclusion criteria: RDC for major depressive disorder (probable or definite), 15+ | Fluvoxamine versus imipramine (50mg -> 100mg on day 5, up to ? on day 8, mean | 1. Leaving the study early due to side effects. 2. Leaving the study early. | This study is included in Amin 1984 (data not extractable) but is not one of the centres | B |

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| | Active Treatment: 4 weeks. | HRSD. Age: 18-65. N=91, HRSD analysis: N=88. Country: UK. Setting: Outpatients. | in wk 4 =153.3) versus placebo. | | included in Kasper 1995. | |
| O'Flynn 1991 | Allocation: Random (no details). Duration: 4 weeks. Analysis: ITT. | Outpatients. N=12; 50% female. Age: 34-56. Diagnosis: DSM-III-R major depression - unipolar, nonpsychotic, HRSD≥17. | Fluoxetine (20mg) versus placebo | 1. Non-responders (patients not achieving ≥ 50% decrease in HRSD). 2. Non-remitters (patients not achieving HRSD≤7). HRSD mean endpoint scores. | All patients underwent a desipramine/ growth hormone stimulation test prior to treatment. | B |
| Ravindra 1995 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: ITT (≥11 days treatment). Active treatment: 8 weeks. | Inclusion criteria: DSM-III-R major depression (mild to moderate severity), 15+ on HRSD. Age: 18-65. N=103, HRSD analysis: N=86. Country: Canada. Setting: Outpatients. | Sertraline versus desipramine (50-225mg, mean after week 4=163.75mg) versus placebo. | 1. Leaving the study early. 2. Leaving the study due to side effects. 3. Patients reporting side effects. | | B |
| Reimherr 90 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: ITT. Active Treatment: 8 weeks. | Inclusion criteria: DSM-III-R major depressive episode, 18+ HRSD (18) without 25% reduction during washout, higher score on Raskin than Covi. Age: 18-65. N=448, HRSD analysis: N= 376. Country: US. Setting: Outpatients. | Sertraline (50-200mg, mean=145mg) versus amitriptyline (50mg, up to 150mg by day 21, mean = 111mg) versus placebo. | 1. HRSD mean change scores.* 2. Leaving the study early. 3. Leaving the study early due to side effects. 4. Non-responders (patients not achieving ≥50% decrease in HRSD). | *extracted data for the "all patients" group. | B |
| Rickels 1986 | Allocation: Random (no details). Duration: 5 weeks Analysis: ITT | N=42; 79% female. Age: 21-70, mean= 47.2+-13. Diagnosis: DSM-III | 1. Fluoxetine (20-80mg). 2. Placebo. | 1. Non-responders (patients not achieving ≥ 50% decrease in HRSD). | | B |

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| | | unipolar major depressive disorder, HRSD≥20, Raskin≥8. | | 2. Leaving the study early.<br>3. Patients reporting side effects. | | |
| Rickels 1989 | Double Blind RCT<br>Concealment of Allocation: unclear.<br>Analysis: ITT..<br>Active treatment: 6 weeks. | Inclusion criteria: DSM-III-major depression, 18+ on HRSD-17; mean baseline HRSD: 26 (+-5). N=111; 62% female. Mean age: 44.<br>Country: US.<br>Setting: Outpatient. | Paroxetine (mean 40 [+-10]) versus placebo. (Allowed chloral hydrate for insomnia in first 2 weeks). | 1. Non-responders (patients not achieving ≥50% reduction in HRSD).<br>2. Leaving the study early.<br>3. Leaving the study early due to side effects.<br>4. Patients reporting side effects. | | B |
| Rickels 1992 | Double Blind RCT<br>Concealment of Allocation: unclear.<br>Analysis: Completer.<br>Active treatment: 6 weeks. | Inclusion criteria: DSM-III-major depression, 18+ on HRSD-17; mean baseline HRSD: paroxetine 26.8 (SE+-0.77), placebo 25.9 (SE+-0.73). N=111; 53 female. Mean age: 43.4 (paroxetine); 46 (placebo).<br>Country: US.<br>Setting: Outpatient | Paroxetine (mean 31.5 [SE+-1.25]) versus placebo. (Allowed chloral hydrate for insomnia in first 2 weeks). | 1. Non-responders (patients not achieving ≥50% reduction in HRSD).<br>2. Leaving the study early.<br>3. Leaving the study early due to side effects (efficacy sample only - data not available for large number of participants due to concomitant medication). | | B |
| Roth90 | Double Blind RCT<br>Concealment of Allocation: Unclear.<br>Analysis: ITT (≥3 weeks treatment).<br>Active treatment: 6 weeks. | Inclusion criteria: DSM-III-R major depressive episode, 22+ HRSD.<br>Age: 18+. N=90, HRSD analysis: N=80.<br>Country: US.<br>Setting: Outpatients. | Fluvoxamine versus desipramine (50mg -> 100mg by day 14, 100-300mg thereafter, mean at wk 3 =195.8mg, mean at wk 6 =224.6) versus placebo. | 1. HRSD mean endpoint scores.<br>2. Leaving the study early. | | B |
| Rudolph 99 | Double blind RCT<br>Concealment of Allocation: Unclear.<br>Analysis: ITT.<br>Active | Inclusion criteria: DSM-IV major depressive disorder, HRSD-21 ≥ 20.<br>Age: 18-40, | Fluoxetine (20-60mg, mean = 47mg) versus venlafaxine XR (75-225mg, mean = 175mg). | 1. HRSD-21 mean endpoint scores.<br>2. Non-responders (patients not achieving ≥50% | | B |

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| | Treatment: 8 weeks. | mean=40. Country: US. Setting: outpatient. | | decrease in HRSD). 3. Non-remitters. 4. Leaving the study early. 5. Leaving the study early due to side effects. | | |
| Sil'stne99 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: ITT. Active treatment: 12 weeks. | Inclusion criteria: DSM-IV major depressive disorder, HRSD-17 ≥ 20. Age: 18-71. Country: UK Setting: Outpatients. | Fluoxetine versus venlafaxine SR (mean = 111.2mg in week 4). | 1. HRSD mean endpoint scores. 2. Leaving the study early. 3. Non-responders (patients not achieving ≥50% decrease in HRSD). 4. Leaving the study early due to side effects. 5. Patients reporting side effects. | | B |
| Smith 1992 | Double Blind RCT Concealment of Allocation: unclear. Analysis: ITT. Active treatment: 6 weeks. | Inclusion criteria: DSM-III major depression, 18+ on HRSD-17; mean baseline HRSD: paroxetine 28.6 (SE+-0.77), placebo 28.9 (SE+-0.77). N=77; female: Paroxetine 44%, placebo 55%. Mean age: 44. Country: US. Setting: Classified as 'mixed' as not clear. | Paroxetine (mean 33.8 mg/day) versus placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | | B |
| Sramek 95 | Allocation: Random (no details). Duration: 9 weeks (+1 week washout). Analysis: LOCF | N=216. Age: 18-65. Diagnosis: DSM-III-R major depressive disorder, HRSD-24≥21. | 1. Fluoxetine (20mg). 2. Placebo 3. ABT-200. | 1. HRSD mean change scores. 2. Leaving the study early. 3. Leaving the study early due to side effects. | | B |
| Stahl 00 | Allocation: Random (no details). Duration: 24 weeks (+ 1week placebo | Inpatients and outpatients. N=323. Age: 18-60. Diagnosis: DSM-IV major | 1. Citalopram (20mg up to 60mg). 2. Sertraline. 3. Placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. 3. Patients | Conducted at eight centres in the US. | B |

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| | washout). Analysis: LOCF. | depressive disorder, HRSD-17≥22. Baseline scores: Citalopram - MADRS=32.4, HRSD-21=26.5. Placebo - MADRS=31.1, HRSD-21=26.4. | | reporting side effects. | | |
| Stark 85 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: ITT (≥ 1 post baseline assessment). Active treatment: 6 weeks. | Inclusion criteria: DSM-III unipolar major depressive disorder for 4 weeks, 20+ HRSD (21), less than 20% reduction in HRSD during wash out period, 8+ on Raskin Scale, and greater than Covi scale. Age: 18-70. N=540, HRSD analysis: N=539. Country: US. Setting: Outpatients. | Fluoxetine versus imipramine (125mg at day 4, up to 300mg thereafter) versus placebo. | 1. Leaving the study early. 2. Leaving the study early due to side effects. | | B |
| Thakore 1995 | Allocation: Random (no details). Duration: 4 weeks. Analysis: ITT. | Outpatients (83%) and inpatients. N=12; 50% female. Age: 18-65, mean = 44.3. Diagnosis: DSM-III-R major depression, HRSD≥17. | Fluoxetine (20mg) versus placebo | 1. HRSD mean endpoint scores. | All patients underwent dexamethosone-induced growth hormone stimulation before randomisation. | B |
| Valducci 1992 | Allocation: Random (no details). Duration: 8 weeks. Analysis: ITT. | Setting: unclear. N=40; 23 female. Age: 19-67. Diagnosis: DSM-III-R major depression, HRSD≥18. | 1. Fluoxetine (20mg) 2. Placebo. | 1. Non-responders (patients not achieving ≥50% decrease in HRSD). 2. Patients reporting side effects. | | B |
| Walczak 1996 | Double Blind RCT Concealment of Allocation: Unclear. Analysis: | Inclusion criteria: DSM-III-R major depressive disorder. Age: 31-50. | 1.Fluvoxamine (25 mg) 2.Fluvoxamine (50 mg) 3.Fluvoxamine (100 mg; mean | 1. Leaving the study early. 2. Leaving the study early due to side effects. | | B |

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| | Completer. Active treatment: 7-8 weeks. | N=600, HRSD analysis: N=351. Country: US. Setting: mixed participants recruited from ten independent centres. | at week 6=100mg) 4. Fluvoxamine (150 mg; mean at week 6=149.22mg) versus Placebo Data extracted only for 150mg dose group. | | | |
| Wernicke 1987 | Allocation: Random (no details). Duration: 6 weeks. Analysis: LOCF | Outpatients. Age: 18-65, mean=39.8. N=356, HRSD analysis: N=345. Diagnosis: DSM-III unipolar major depressive disorder, HRSD≥20, Raskin depression score > Covi anxiety score. | 1. Fluoxetine (20mg). 2. Fluoxetine (40mg). 3. Fluoxetine (60mg). 4. Placebo. | 1. HRSD mean change scores (20mg only). 2. Non-responders (patients not achieving ≥50% decrease in HRSD). 3. Leaving study early. 4. Leaving study early due to side effects. | Dichotomous data is combined for 20, 40 and 60mg groups. | B |
| Wernicke 1988 | Allocation: Random (no details). Duration: 6 weeks (+1 week washout). Analysis: ITT (≥1 post-baseline assessment). | Outpatients. N=363; HRSD analysis: 61% female. Age: 18-65, mean=39. Diagnosis: DSM-III unipolar depression, HRSD≥20. | 1. Fluoxetine (5mg). 2. Fluoxetine (20mg). 3. Fluoxetine (40mg). 4. Placebo. | 1. HRSD mean change scores (20mg only). 2. Non-responders (patients not achieving ≥50% decrease in HRSD). 3. Leaving study early. 4. Leaving study early due to side effects. | Dichotomous data is combined for 20 and 40mg groups. | B |

## Characteristics of excluded studies

| Study | Reason for exclusion |
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| Anisman 1999 | 100% dysthymics. |
| Bakish 2000 | No placebo arm. |
| Bastos 1996 | Not an RCT (in Portuguese - paper evaluated by native speaker). |
| Baumann 1996 | Not a relevant comparison (all patients were treated with citalopram then randomised to receive additionally placebo or lithium if they were unresponsive). |
| Bhagwagar 2002 | Not a relevant comparison (compared depressed patients with recovered patients with healthy controls). |
| Brunner 1994 | No placebo control group. |
| Cetin 1994 | Paper is in Turkish; unable to assess eligibility. |
| Cook 1999 | All patients were receiving supportive psychotherapy. |
| Corrigan 2000 | Patients on psychotherapy or behaviour therapy were allowed to continue whilst taking part in the study, number not specified, therefore unable to determine whether there was an even distribution between treatment groups of patients receiving therapy. |
| Danjou 1994 | No placebo arm. |
| Davidson 02 | Inadequate dose of sertraline (50-100mg). |
| Doogan 1994 | Patients on inadequate dose of sertraline (only 24% received ≥100mg). |
| Evans 1997 | Inadequate diagnosis of depression. |
| Fabre 1985 | Inadequate diagnosis of depression. |
| Fieve 1986 | No extractable data. |
| Gacgoud 1992 | No placebo control group. |
| Golden02 | Unable to ascertain how many patients were randomised to each treatment group, therefore unable to extract any data. |
| Gottfries 1992 | Inadequate diagnosis and some patients with dementia. |
| Guy 1986 | Not clear if randomised; very small sample (N=4 for placebo arm). |
| Harto 1988 | No extractable data. |
| Heiligenstein 1993 | Patients were classified as unipolar depressed or bipolar type II depressed according to RDC, number of bipolar patients not specified. |
| Hellerstein 2000 | 100% dysthymics. |
| Hoch'sser 01 | Maintenance phase treatment only. |
| Hochberg 1995 | 1 year extension to a 6-week trial on cardiographic findings. Unable to locate publication of acute phase trial. |
| Johnson 1993 | No extractable data |
| Kerr 1993 | No placebo arm. |
| Kiev 1992 | Unable to ascertain how many patients were randomised to each treatment group, therefore unable to extract any data. |
| Klysner 02 | Maintenance treatment phase only. |
| Lam 1995 | Patients were diagnosed with recurrent major depressive episode with a seasonal pattern. |
| Lundbeck 1995 | Unable to locate published report. |
| Mont'mery93 | Maintenance treatment phase only. |
| Montgomery 1988 | Maintenance phase study. All patients in acute phase received fluoxetine. |
| Moon 1993 | Abstract only. Unable to obtain full publication. |
| New 1999 | No extractable data. |
| Nyth 1992 | Inadequate diagnosis and 19% of patients had comorbid dementia. |
| Olie 1997 | Unclear whether patients received an adequate dose of sertraline ("83% received doses of either 50mg or 100mg"). 88% of sertraline group and 89% of placebo group on concomitant medication, including benzodiazepines. |
| Pande 1999 | Unable to establish number of patients randomised to each group. |
| Peselow 1986 | Paper gives results of two trials combined (sertraline v placebo and oxaprotiline v placebo) - not possible to separate results by active drug. |

| | |
|---|---|
| Puzynski 1994 | Paper is in Polish; unable to assess eligibility. |
| Rausch 2002 | No placebo arm. |
| Ravindran 1999 | 100% dysthymics |
| Reimherr 1984 | Fluoxetine results from the double blind study are combined with those from an open trial. |
| Reynaert 1993 | No placebo arm. |
| Robert 1995 | Maintenance treatment phase only. |
| Ruhrmann 1998 | No placebo arm. |
| Sacchetti 1997 | No placebo control group. |
| Schneider03 | Some participants on HRT. |
| Thompson 1991 | Patients on inadequate dose of sertraline (only 27% received ≥100mg). |
| Thompson 1994 | Sertraline given at sub-therapeutic dose - 76% patients on 50mg. |
| Tollefson93 | Some participants on HRT. |
| Vanelle 1997 | All patients were diagnosed with dysthymia (not concurrent with major depression). |
| von Bardeleben 1989 | There were only 2/14 patients in the placebo arm. |
| Wade 2002 | No Citalopram arm - Escitalopram versus placebo. |
| Wakelin 1986 | Sub-analysis of elderly patients from Amin1984, Itil1983 and Block1983. |
| White 1990 | Reports results of crossover from Desipramine to Fluvoxamine in Desipramine non-responders. Unable to locate publication of acute phase trial. |

## Appendix H Psychology Search Filters

*1. Guided self-help*

Databases - MEDLINE, CINAHL, EMBASE, PsycINFO

1. bibliotherapy/

2. (self help or self?help or bibliotherap$ or reading therap$ or book therap$ or self?improv$ or self improv$).tw.

3. 1 or 2

AND RCT AND Depression (as for pharmacological searches)

*2. Behaviour therapy (BT)*

Databases - MEDLINE, CINAHL, The Cochrane Controlled Trials Register, EMBASE, PsycINFO, AMED (1985-APRIL 2002)

1. (BEHAVIO$ ADJ THERAP$) or (BEHAVIO$ ADJ (TECHNIQUE$ or THERAP$ or RESTRUCTUR$ )) or (BEHAVIO$ ADJ (ACTIVAT$ or ANALY$))

2. exp BEHAVIOR THERAPY/

3. Behavior therapy/

4. or/1-3

AND Depression AND RCT NOT CBT (as for pharmacological searches)

*3. Cognitive behavioural therapy (CBT)*

Databases - The Cochrane Controlled Trials Register, EMBASE, MEDLINE, PsycINFO, CINAHL, AMED

1. (COGNITIV* and BEHAVIO* and THERAP*)

2. ((COGNITIV$ ADJ (BEHAVIO$ or ANALY$) ADJ THERAP$) or (COGNITI$ ADJ (TECHNIQUE$ or THERAP$ or RESTRUCTUR$ or CHALLENG$)) or (COGNITIV$ ADJ BEHAVIOR$ ADJ ANALY$ ADJ SYSTEM$) or (BEHAVIO$ and (ACTIVAT$ or ANALY$)))

3. (exp COGNITIVE THERAPY/)

4. cognitive therapy/

5. (BEHAVIO$ ADJ (ACTIVAT$ or ANALY$))
6. or/1-5

AND Depression AND RCT (as for pharmacological searches)

*4. Interpersonal psychotherapy (IPT)*

Databases - The Cochrane Controlled Trials Register, EMBASE, MEDLINE, PsycINFO, CINAHL, AMED

1. (interpersonal or inter-personal) adj (therap$ or psychotherap$)

AND Depression AND RCT NOT CBT (as for pharmacological searches)

*5. Counselling*

Databases - The Cochrane Controlled Trials Register, EMBASE, MEDLINE, PsycINFO, CINAHL, AMED

1. (((counsel$) or ((support$ or rogerian) adj (therap$ or psychotherapy)) or ((exploratory or non-directive) adj25 psychotherapy)) or ('counseling-' / all subheadings)))
2. exp counselling/
3. exp Supportive Psychotherapy/
4. counseling/
5. or/1-4

AND Depression AND RCT NOT CBT (as for pharmacological searches)

*6. Problem-solving therapy*

Databases - The Cochrane Controlled Trials Register, EMBASE, MEDLINE, PsycINFO, CINAHL, AMED

1. (problem adj solving) or (coping adj (strateg$ or skill$)) adj25 (therap$ or train$ or intervention$)
2. Exp problem solving/
3. problem solving/

4. or/1-3

AND Depression AND RCT NOT CBT (as for pharmacological searches)

*7. Short-term psychodynamic psychotherapy*

Databases - The Cochrane Controlled Trials Register, EMBASE, MEDLINE, PsycINFO, CINAHL, AMED

1. (PSYCHOANALY* or ((ANALYTIC* or DYNAMIC* or PSYCHODYNAMIC*) and (THERAP* or PSYCHOTHERAP*)))

2. ((psychoanaly*) or ((analytic* or dynamic* or psychodynamic*) near2 (therap* or psychotherap* ))or ('PSYCHOANALYSIS-'/ all subheadings))

3. ((exp PSYCHOANALYSIS/ or exp Psychoanalytic Therapy/) or (psychoanaly$ or ((analytic$ or dynamic$ or psychodynamic$) adj2 (therap$ or psychotherap$)))

4. (exp Psychoanalysis/ or (psychoanaly$ or ((analytic$ or dynamic$ or psychodynamic$) adj2 (therap$ or psychotherap$))))

5. ((Psychoanalytic Therapy/) or (psychoanaly$ or (analytic$ or dynamic$ or psychodynamic$) adj2 (therap$ or psychotherap$)))

6. or/1-5

AND Depression AND RCT NOT CBT (as for pharmacological searches)

## Appendix I Included and Excluded Studies – Psychology

### *References to included studies*

* indicates the primary reference for the study


**BEACH 1986 (US)** {published data only}
Beach SR, O'Leary KD. The treatment of depression occurring in the context of marital discord. Behavior Therapy 1986;17(1):43-49.

**BEACH 1992 (US)** {published data only}
Beach SRH, O'Leary KI. Treating depression in the context of marital discord: outcome and predictors of response of marital therapy versus cognitive therapy. Behav Ther 1992;23:507-528.

**BEDI 2000 (UK)** {published data only}
* Bedi N, Chilvers C, Churchill R, Dewey M, Duggan C, Fielding K, Gretton V, Miller P, Harrison G, Lee A, Williams I. Assessing effectiveness of treatment of depression in primary care. Partially randomised preference trial. British Journal of Psychiatry 2000;177:312-318.
Chilvers,C.; Dewey,M.; Fielding,K.; Gretton,V.; Miller,P.; Palmer,B.; Weller,D.; Churchill,R.; Williams,I.; Bedi,N.; Duggan,C.; Lee,A.; Harrison,G.. Antidepressant drugs and generic counselling for treatment of major depression in primary care: randomised trial with patient preference arms.. BMJ 2001;322:1-5.

**BELLAMY 2000 (UK)** {published data only}
Bellamy A, Adams B. An evaluation of the clinical effectiveness of a counselling psychology service in primary care. Counselling Psychology Review 2000;15(2):England, http.

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*Beutler LE, Engle D, Mohr D, Daldrup RJ, Bergan J, Meredith K, Merry W. Predictors of differential response to cognitive experiential and self-directed psychotherapeutic procedures. Journal of Consulting and Clinical Psychology 1991;59:333-340.
Rosner R,Frick U,Beutler LE,Daldrup R.Course of depression in different psychotherapies - An application of hierarchical linear models.Zeitschrift fur Klinische Psychologie 1999;28(2):112-20

**BLACKBURN 1981 (UK)** {published data only}
* Blackburn IM, Bishop S, Glen AIM, Whalley LJ, Christie JE. The efficacy of cognitive therapy in depression: a treatment trial using cognitive therapy and pharmacotherapy each alone and in combination.. Br J Psychiatry 1981;139:181-189.

Blackburn,I.M.; Euson,K.; Bishop,S.. A 2-year naturalistic follow-up of depressed patients treated with cognitive therapy, pharmacotherapy and a combination of both. [A 2-year naturalistic follow-up of depressed patients treated with cognitive therapy, pharmacotherapy and a combination of both.]. J.Affect.Disord. 1986;10:67-75.

**BLACKBURN 1997 (UK)** {published data only}
Blackburn IM, Moore RM. Controlled acute and follow-up trial of cognitive therapy and pharmacotherapy in out-patients with recurrent depression. British Journal of Psychiatry 1997;171:328-334.

**BOWMAN 1995** {published data only}
Bowman D,Scogin F,Lyrene B.The efficacy of self-examination therapy & cognitive bibliotherapy in the treatment of mild to moderate depression. Psychotherapy Research 1995;5(2):131-140.

**BROWN 1984** {published data only}
Brown RA, Lewinsohn PM. A psychoeducational approach to the treatment of depression: Comparison of group, individual, and minimal contact procedures. Journal of Consulting & Clinical Psychology 1984;52(5):774-783.

**BRIGHT 1999 (US)** {published data only}
Bright JI, Baker KD, Neimeyer RA. Professional and paraprofessional group treatments for depression: a comparison of cognitive-behavioral and mutual support interventions. Journal of Consulting & Clinical Psychology 1999;67(4):491-501.

**BURNAND 2002 (Swiss)** {published and unpublished data}
Burnand Y, Andreoli A, Kolatte E, Venturini A, Rosset N. Psychodynamic psychotherapy and clomipramine in the treatment of major depression. Psychiatric Services 2002;53(5):585-590.

**COVI 1987 (US)** {published data only}
Covi L, Lipman RS. Cognitive behavioral group psychotherapy combined with imipramine in major depression.. Psychopharmacol Bull 1987;23(1):173-176.

**DE MELLO 2001(BRAZ)** {published data only}
de Mello MF, Myczcowisk LM, Menezes PR. A randomized controlled trial comparing moclobemide and moclobemide plus interpersonal psychotherapy in the treatment of dysthymic disorder. Journal of Psychotherapy Practice & Research 2001;10(2):117-123.

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Derubeis RJ, Hollon SD, Amsterdam JD, Shelton RC, Young PR, Salomon RM, O'Reardon JP, Lovett ML, Gladis MM, Brown LL, Gallop R (2005),

Cognitive therapy vs medications in the treatment of moderate to severe depression, Arch.Gen.Psychiatry 62: 409-416

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Dimidjian S, Hollon SD, Dobson KS, Schmaling KB, Kohlenberg RJ, Addis ME, Gallop R, McGlinchey JB, Markley DK, Gollan JK, Atkins DC, Dunner DL, Jacobson NS (2006), Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression, J Consult Clin Psychol. 74: 658-670

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* Dowrick C, Dunn G, Ayuso-Mateos JL, Dalgard OS, Page H, Lehtinen V, Casey P, Wilkinson C, Vazquez-Barquero JL, Wilkinson G, Birkbeck G, Borve T, Costello M, Cuijpers P, Davies I, Fenlon N, Finne M, Ford F, Del Barrio AG, Hayes C, Horgan A, Koffert T, Jones N, Lasa L, Lehtila M, McDonough C, Michalak E, Murphy C, Nevra A, Nummelin T, Sohlman B. Problem solving treatment and group psychoeducation for depression: Multicentre randomised controlled trial. BMJ 09 DEC 2000Vol 321(7274) ()(pp 1450-1454), 2000 2000;(7274):1450-1454.
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Agosti V, Ocepek-Welikson K. The efficacy of imipramine and psychotherapy in early-onset chronic depression: a reanalysis of the National Institute of Mental health Treatment of Depression Collaborative Research Program. Journal of Affective Disorders 1997;43:181-186.

**FRANK 1990 (US)** {published data only}
* Frank E, Kupfer DJ, Perel JM, Cornes C, Jarrett DB, Mallinger AG, Thase ME, McEachran AB, Grochocinski VJ. Three-year outcomes for maintenance therapies in recurrent depression. Archives of General Psychiatry 1990;47(12):1093-1099.

**FREEMAN2002 (UK)** {unpublished data only}
Freeman, C.P.L., Power, M.J., Bowyer, D.J., Law, R.. Breif structured psychotherapies for neurotic disorders in primary care: a comparison of CBT, PT and treatment as usual at early and late intervention.

**GALLAGHER 1983 (US)** {published data only}

Gallagher DETLW. Effectiveness of psychotherapy for both endogenous and nonendogenous depression in older adult outpatients.. J Gerontol 1983;38:707-712.

**GALLAGHER-TH 94 (US)** {published data only}
Gallagher-Thompson DE, Steffen AM. Comparative effects of cognitive behavioral therapy and brief psychodynamic psychotherapies for depressed family caregivers.. J Consult Clin Psychol 1994;62(3):543-549.

**GARLAND 2000 (UK)** {published data only}
Garland A, Harrington J, House R, Scott J. A pilot study of the relationship between problem-solving skills and outcome in major depressive disorder. British Journal of Medical Psychology 2000;73(3):303-309.

**HOLLON 1992 (US)** {published data only}
* Hollon SD, DeRubeis RJ, Evans MD, Wiemer MJ, Garvey MJ, Grove WM, Tuason VB. Cognitive therapy and pharmacotherapy for depression. Arch Gen Psychiatry 1992;49:774-781.
Evans,M.D.; Hollon,S.D.; DeRubeis,R.J.; Piasecki,J.M.; Grove,W.M.; Garvey,M.J.; Tuason,V.B.. Differential relapse following therapy and pharmacotherapy for depression.. Archives of General Psychiatry 1992;49:802-808.

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Luborsky L, Diguer L, Cacciola J, Barber JP, Moras K, Schmidt K, DeRubeis RJ. Factors in outcomes of short-term dynamic psychotherapy for chronic vs. nonchronic major depression. Journal of Psychotherapy Practice & Research 1996;5(2):152-159.

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Scogin F. Comparative efficacy of cognitive and behavioral bibliotherapy for mildly and moderately depressed older adults. Journal of Consulting & Clinical Psychology 57(3):403-7, 1989.

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* Shapiro DA, Barkham M, Rees A, Hardy GE, Reynolds S, Startup M. Effects of treatment duration and severity of depression in the maintenance of gains following cognitive/behavioural and psychodynamic/interpersonal psychotherapy.. J Consult Clin Psychology 1994;62(3):522-534.

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Simpson S, Corney R, Fitzgerald P, Beecham J. A randomized controlled trial to evaluate the effectiveness and cost-effectiveness of psychodynamic counselling for general practice patients with chronic depression. Psychological Medicine 33(2):229-39, 2003.

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Steuer JL, Mintz J, Hammen CL, Hill MA, Jarvik LF, McCarly T, Motoike P, Rosen R. Cognitive-behavioral and psychodynamic group psychotherapy in treatment of geriatric depression.. J Consult Clin Psychol 1984;52(2):180-189.

**STRAVYNSKI 1994 (Ca)** {published data only}
Stravynski A, Verreault R, Gaudette G, Langlois R, Gagnier S, Larose M. The treatment of depression with group behavioural-cognitive therapy and imipramine. Canadian Journal of Psychiatry 1994;39(7):387-390.

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* Thompson,L.W.; Coon,D.W.; Gallagher-Thompson,D.; Sommer,B.R.; Koin,D.. Comparison of desipramine and cognitive/behavioral therapy in the treatment of elderly outpatients with mild-to-moderate depression. American Journal of Geriatric Psychiatry 2001;9(3):225-240.

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Tschuschke V, Anbeh T. Early treatment effects of long-term outpatient group therapies - First preliminary results. Group Analysis 2000;33(3):397-411.

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Ward E, King M, Lloyd M, Bower P, Sibbald B, Farrelly S, Gabbay M, Tarrier N, Addington-Hall J. Randomised controlled trial of non-directive counselling, cognitive-behaviour therapy, and usual general practitioner care for patients with depression. I: clinical effectiveness. [see comments.]. BMJ 2-12-2000;321(7273):1383-1388.

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Weissman MM, Prusoff B, Sholomskas AJ, Greenwald S. A double-blind clinical trial of alprazolam, imipramine, or placebo in the depressed elderly. Journal of Clinical Psychopharmacology 1992;12(3):175-182.

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Wilson GL. Psychotherapy with depressed incarcerated felons: a comparative evaluation of treatments.. Psychol Rep 1990;67:1027-1041.

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## *References to excluded studies*

* indicates the primary reference for the study


**ALEXOPOULOS 2003 {published data only}**

Alexopoulos GS, Raue P, Arean P. Problem-solving therapy versus supportive therapy in geriatric major depression with executive dysfunction. American Journal of Geriatric Psychiatry 2003;11(1):46-52.

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**BARKHAM 1996 (UK)** {published data only}

Barkham M, Rees A, Shapiro DA, Stiles WB, Agnew RM, Halstead J, Culverwell A, Harrington VM. Outcomes of time-limited psychotherapy in applied settings: replicating the Second Sheffield Psychotherapy Project. [letter; comment.]. Journal of Consulting & Clinical Psychology 1996;64(5):1079-1085

**BECK 1985 (US)** {published data only}

Beck AT, Hollon SD, Young JE, Bedrosian RC, Budenz D. Treatment of depression with cognitive therapy and amitriptyline. Arch Gen Psychiatry 1985;42:142-148.

**BELLAMY 2000 (UK)** {published data only}

Bellamy A, Adams B. An evaluation of the clinical effectiveness of a counselling psychology service in primary care. Counselling Psychology Review 2000;15(2):England, http.

**BEUTLER 1991** {published data only}

*Beutler LE, Engle D, Mohr D, Daldrup RJ, Bergan J, Meredith K, Merry W. Predictors of differential response to cognitive experiential and self-directed psychotherapeutic procedures. Journal of Consulting and Clinical Psychology 1991;59:333-340.

Rosner R,Frick U,Beutler LE,Daldrup R.Course of depression in different psychotherapies - An application of hierarchical linear models.Zeitschrift fur Klinische Psychologie 1999;28(2):112-20

**BLENKIRON 2001** {published data only}

Blenkiron P. Coping with depression: A pilot study to assess the efficacy of a self-help audio cassette. British Journal of General Practice 51(466):366-70, 2001.

**BOLTON 2001 (Aust)** {published and unpublished data}
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Bowers WA. Treatment of depressed in-patients. Cognitive therapy plus medication, and medication alone.. Br J Psychiatry 1990;156:73-78.

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Catalan J, Gath DH, Anastasiades P, Bond SA, Day A, Hall L. Evaluation of a brief psychological treatment for emotional disorders in primary care. Psychological Medicine 1991;21(4):1013-1018.

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Donnan P, Hutchinson A, Paxton R, Grant B, Firth M. Self-help materials for anxiety: a randomized controlled trial in general practice. Brit.Journal of General Practice 1990;40:498-501.

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Dunn RJ. Cognitive modification with depression-prone psychiatric patients.. Cogn Ther Res 1979;3(3):307-317.

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Dunner DL, Schmaling KB, Hendrickson H, Becker J, Lehman A, Bea C. Cognitive therapy versus fluoxetine in the treatment of dysthymic disorder. Depression 1996;4(1):34-41.

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Fleming BM, Thornton DW. Coping skills training as a component in the short-term treatment of depression. Journal of Consulting & Clinical Psychology 1980;48(5):652-654.

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## Appendix J Characteristics of Included Studies – Psychology

**Notes on the use of the Tables**

**Methods** - describes the design of the trial including details of randomisation and blinding, the duration of the trial and whether analysis of continuous data was carried out on an intention-to-treat or completer sample.In some cases intention-to-treat may not refer to the number of patients originally randomised to each treatment group since many studies defined their own criteria, commonly that patients included in the intention-to-treat sample must have received at least one dose of study drug, and undergone at least one assessment.

**Participants** - details of the patients who entered trials and the criteria for their inclusion in the study, patient setting, number of patients randomised, age range or mean age, number of female participants, diagnostic inclusion criteria and baseline depression scale scores, country in which the trial took place. This information refers to the total number of patients randomised in a study; where there were more than two treatment groups it may not relate to the patients entered into the review.

**Interventions** - lists all the treatment groups that patients could be assigned to; in pharmacological trials the dose range or mean dose administered to patients is given. In trials with more than two treatment arms a note is made of which groups were used in the review.

**Outcomes** - lists the outcomes which have been extracted including how 'response' and 'remission' have been defined by individual studies where appropriate.

**Notes** - contains additional information, for example, where the study was carried out and by whom, and mean baseline depression scale scores.

**Allocation concealment (AC)** - grades studies from A-D according to how well treatment group assignment was concealed from investigators and patients. 'A' indicates concealment was adequate, 'B' unclear, 'C' inadequate, and 'D' indicates that allocation concealment was not used as a criterion to assess validity.

The following abbreviations are used:

| | | |
|---|---|---|
| AD = antidepressant | CT = cognitive therapy | OT = occupational therapist |
| BDI = Beck Depression Inventory | DSM = Diagnostic Statistical Manual | PST = problem solving therapy |
| BMT = behavioural marital therapy | HRSD = Hamilton Rating Scale for Depression | RDC = Research Diagnostic Criteria |
| BT = behaviour therapy | ICD = International Classification of Diseases | SADS = Schedule for Affective Disorders and Schizophrenia |

| | | |
|---|---|---|
| CBT = cognitive behavioural therapy | IPT = interpersonal therapy | SCL-R = Depression Symptom Check List |
| CIS = Clinical Interview Schedule | ITT = intention-to-treat | SDAS-L = |
| CM = clinical management | LOCF = last observation carried forward | TAU = treatment as usual |
| CPN = community psychiatric nurse | MMPI = Minnesota Multi-phasic Inventory | WLC = wait list control |

## Guided self-help

### Characteristics of included studies

| Study | Methods | Participants | Interventions | Outcomes | Notes | AC |
|---|---|---|---|---|---|---|
| Beutler 1991 | Allocation: random (no details). Duration: 20 weeks +3-month follow-up. Analysis: Patients who remained in treatment for at least four sessions (LOCF). | Outpatients with moderate depression, recruited via press, word of mouth and professional recommendation who were willing to discontinue all other pharmacological or psychological treatments. N=76, five patients were excluded after it was found they had not withdrawn from other mental health treatments therefore study analysis was based on 71 patients. 67% female. Mean age: 46.76. Diagnosis: DSM-III major depressive disorder and HRSD>=16. | 1. Group CBT - following Yost *et al.* (1986) and Beck *et al.* (1979). 2. Focused expressive psychotherapy - a Gestalt-based group psychotherapy supplemented by homework assignments. 3. Supportive self-directed therapy - weekly telephone contacts of 30 mins each and reading prescribed books. Group size 5 - 10 members | 1. BDI mean scores at endpoint. 2. BDI mean scores at 3-month follow-up. 3. HRSD mean scores at endpoint. 4. HRSD mean scores at 3-month follow-up. | Therapists were four experienced psychologists trained in CT and focused expressive psychotherapy. Five advanced graduate students conducted supportive self-directed therapy. | B |
| Bowman 1995 | Allocation: random. Duration of study: 4 weeks + 2-month follow-up | Included community-dwelling individuals who scored >=10 on HRSD-21, were not in | 1. Cognitive bibliotherapy: Participants received "Feeling Good" (Burns, 1980). Participant received weekly calls from a researcher to evaluate progress and to offer help | 1. HRSD mean scores at endpoint. 2. HRSD mean scores at 2-month follow-up | Country of study: US. Two participants who dropped out before post-treatment | B |

| | | | | | | |
|---|---|---|---|---|---|---|
| | assessment. Analysis: completer. | psychotherapy at the time of the study, not receiving pharmacotherapy and not evidencing or reporting psychosis, suicidal risk or mania. N = 32; 62.5% female. Mean age: 36.2 years. Diagnosis: HRSD>=10. | in interpreting anything about the book that was unclear. 2. Self-examination therapy: Participants received a 39-page booklet that encouraged participants to isolate themselves at home for at least 30 minutes each week to decide what was relevant to their lives and record this on a sheet. The book suggested using a flow-chart format to attempt to address their difficulties. The book encouraged discarding problems that did not matter to them and to brainstorm for solutions for problems that did matter to them. 3 WLC: Participants received weekly calls from researchers assuring them that treatment would become available. Following a 4-week waiting period, they were randomised to either of the first two treatments (data extracted for 4-week study period only). | (interventions 1 & 2 only). 2. BDI mean scores at endpoint. 3. BDI mean scores at 2-month follow-up (interventions 1 & 2 only). 3. Leaving the study early. | assessment were replaced. | |
| Brown 1984 | Allocation: Random. Duration: 8 weeks + 1 month and 6-month follow-ups. Analysis: ITT. | Individuals responding to an announcement for "Coping with Depression". N = 80. Study analyses were based on a subsample of 63 participants who met RDC criteria for unipolar depression. 70% female. Mean age 36.5 years (range 16-65 years). Diagnosis: SADS-RDC diagnosis: major depressive (44% patients) disorder, minor depressive disorder (11% patients), intermittent | 1. Class psychoeducation (or group bibliotherapy): Two classes of nine in the first cohort and two classes of seven in the second. Classes were co-taught by two instructors. Lecturing supplemented course readings and homework assignments were reviewed. Participants were asked to share experiences in doing homework. Cohesiveness among participants was promoted. Duration of session: 2 hours. 2. Individual psychoeducation (or individual bibliotherapy): Similar to class condition, but consisted of individual tutoring sessions. Duration of session: 50 minutes or less. 3. Telephone contact: | 1. BDI mean scores at endpoint. 2. BDI mean scores at 1-month and 6-month follow-up (interventions 1, 2 & 3 only). 3. Non-remitters (patients still meeting SADS-RDC criteria for depression) at 6-month follow-up (interventions 1, 2 & 3 only). | Country of study: US. Of 63 participants with unipolar depression, 22 were involved in concurrent treatment for depression at the time of initial assessment Four advanced doctoral students in clinical psychology served as instructors. Following the intake interview, participants met with their instructor | B |

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|---|---|---|---|---|---|---|
| | | depressive disorder (44% patients). | Instructors met with participants for one session at beginning of course during which rationale of course was elaborated upon and assignments and monitoring forms explained. All subsequent sessions were conducted via telephone contacts during which participants were encouraged and assisted in completing course assignments. Calls lasted 15 minutes.<br>4. WLC: Following 8-week waiting period, participants received class psychoeducation (data extracted for 8-week study period only).<br>The course employed "Control your depression" by Lewinsohn and a participant workbook by Brown & Lewinsohn, that contained goal statements and assignments for each unit. Three sessions per week were held during first 4 weeks and one per session during second 4 weeks. Skill areas taught in the course were learning how to relax, increasing pleasant activities, changing aspects of one's thinking, and improving social skills and increasing positive social interactions. | | during which instructors became acquainted with participant and presented overview and rationale of the course. | |
| Jamison 1995 | Allocation: Random (no details). Duration of study: 4 weeks treatment phase plus 3-month follow-up. Analysis: completer. | Outpatients. N = 80; 84% female. Mean age: 40. Diagnosis: HRSD-21 >= 10; DSM for mild or moderate major depression - responses to HRSD were examined and determined whether five of nine symptoms required by DSM-III-R were present, including depressed mood or loss of interest | 1. Cognitive bibliotherapy: Patients were requested to read "Feeling Good" (Burns, 1980) within 4 weeks, and given a booklet describing exercises in the book. BDI administered by weekly telephone interviews. Number of exercises were noted at successive interviews.<br>2. WLC: During 4-week waiting period, BDI administered during 10-minute telephone interviews. Received bibliotherapy at end of 4 weeks (data extracted for 4- week study period only). | 1. Leaving the study early.<br>2. HRSD mean endpoint scores.<br>3. BDI mean endpoint scores.<br>4. Non-remitters (patients not achieving HRSD<=12).<br>5. Non-remitters (patients not achieving | Country of study: US. 3-month follow-up data not extracted since control group received bibliotherapy during follow-up interval. | B |

| | | | | | | |
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| | | or pleasure; BDI >= 10 brief screening interview conducted to find out willingness to read a book as the major treatment. | | BDI<=11). | | |
| Landreville 1997 | Allocation: Random (no details). Duration of study: 4 weeks + 6-month follow-up. Analysis: completer. | Volunteers through media, practitioners, and social service professionals (a) aged >=55 years; (b) Geriatric Depression Scale >=11; (c) having one or more disabilities in activities of daily life; (d) living independently in the community N = 44. Study analyses were based on a subsample of 23 patients who had a depression diagnosis and who completed the study (number of patients with a diagnosis of depression originally randomised not given). 87% female. Mean age: 71.8 (bibliotherapy, N=10); 72.15 (control, N=13). 63.63% had physical problems. Diagnosis: DSM-III-R for major depression (N = 17) or DSM-IV for minor depression (N = 6). | 1. Cognitive bibliotherapy: Participants received a copy of "Feeling Good" (Burns, 1980) and asked to read entire book within 4 weeks. An average of 46.66% (range 6.66 to 100%) of the book was read.<br>2 WLC: These participants received 4-week bibliotherapy after the study treatment phase (data extracted for 4-week study period only).<br>Participants in both groups received 15-minute telephone calls once a week by a graduate psychology student in order to assess progress and answer questions about the book in the experimental group, and to monitor condition and to encourage them to persevere until treatment became available in the control group. | 1. BDI mean endpoint scores. | Country of study: Canada. | B |
| Schmidt 1983 | Allocation: Random. Duration of | Individuals with BDI >=10, depression as | 1. Bibliotherapy: Clients met in two small groups with therapist during first | 1. Leaving the study early. | Country of Study: US. | D |

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| | study: 8 weeks treatment phase + 10 week follow-up. Analysis: ITT. | major presenting problem, with a minimum duration for the current episode of 2 weeks, no history of bipolar symptomatology or other psychotic states, absence of suicidal ideation during prior year and absence of suicidal behaviour during past 2 years, payments of a $25 research deposit. N = 56; 84% female. Mean age: 42. Diagnosis: Study conducted shortly before publication of DSM-III and RDC for affective disorders. Retrospective analysis revealed multiple items pertinent to determination of all RDC criteria except "distinct quality of depressed mood". Based on this, five participants had endogenomorphic depression. | week of treatment. Clients received a copy of the self-help manual and were asked to return mood assessment forms every week. The self-help manual was based on "Control your depression" (Lewinsohn *et al.*, 1986), Beck (1976), Alberti & Emmons (1970), and Lange & Jakubowski (1976). Clients received a telephone call during the fourth week aimed at encouraging and answering the client's questions.<br>2. Individual therapy.<br>3. Small group therapy.<br>4. Large group therapy: Clients met with therapist weekly for 90 minutes. Treatment procedures and ways of dealing with client's difficulties were discussed. Earlier sessions concentrated on behavioural methods. Cognitive materials followed, presenting more difficult and introspective assignments. Finally assertion skills were taught by combining introspective and behavioural tasks.<br>5 WLC: Clients were informed that they would receive therapy in about 8 weeks (data extracted for 8-week study period only). | 2. BDI mean scores at endpoint.<br>3. BDI mean scores at 10-week follow-up (interventions 1, 2, 3 & 4 only). | | |
| Scogin 1987 | Allocation: Random (no details). Duration of study: 4 week treatment + 1-month follow-up. Analysis: completer. | Community-dwelling individuals aged >=60 years who could read. N = 29; 79% female. Mean age: 70.8 (cognitive Bibliotherapy); , 71.8 years (WLC); 68.5 (control bibliotherapy). Diagnosis: HDRS | 1. Cognitive bibliotherapy: Participants received a copy of "Feeling Good" (Burns, 1980).<br>2 WLC: Following 1-month waiting period, participants received cognitive bibliotherapy (data extracted for 4-week study period only).<br>All participants undergoing therapy received 10-minute weekly phone calls from researchers that were supportive and involved an | 1. Leaving the study early.<br>2. BDI mean endpoint scores.<br>3. HRSD mean endpoint scores. | Country of study: US. Three in cognitive bibliotherapy and one in WLC were receiving medication prescribed by their physicians. | B |

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| | | >= 10. | informal assessment of the participant's progress. Participants were encouraged to complete the book within 1 month. 3. Control bibliotherapy: Participants received a copy of Frankl's "Man's Search for Meaning" This treatment group started midway through the study in an effort to improve study design. Therefore, not properly randomised. Data not extracted for this treatment. | | | |
| Scogin 1989 | Allocation: Random (no details) Duration of study: 1-month + 6-month follow-up. Analysis: completer | Community-dwelling individuals aged >=60 years recruited via the media. N = 67; 85% female. Mean age: 68.3 years. Diagnosis: HDRS >= 10; Mental Status Questionnaire >=8. | 1. Cognitive bibliotherapy: Participants received a copy of "Feeling Good" (Burns, 1980). 2. Behavioural bibliotherapy: Participants received a copy of "Control your Depression" (Lewinsohn *et al.*, 1986). 3. WLC: At the end of waiting period, participants were randomised to either cognitive or behavioural bibliotherapy (data extracted for 4-week study period only). All participants receiving bibliotherapy received 5-minute weekly telephone calls to assess progress and to answer questions about the reading material. Data was extracted for 1 and 3 only. | 1. Leaving the study early. 2. HRSD mean scores at endpoint. | Country of Study: US. | B |
| Wollersheim 1991 | Allocation: Random, blocked for age and sex (no other details). Clinician's ratings of depression were performed blind to treatment allocation. Duration: 11-week treatment | Outpatients. N = 32; 8 randomised to each group; 72% female. Age: 39.4 years. Diagnosis: DSM-III for depressive disorder. | 1. Bibliotherapy: Patients given Wollersheim's "Bye Bye Blues: Overcoming Depression" Patients also received minimal therapist contact (three meetings). Instructions given to read a specified number of chapters each week. 2. Coping therapy: Used CBT for unipolar depression using Wollersheim, 198 and , 1984 manualas). Ten 2-hour sessions conducted with each session having a different goal aimed at | 1. BDI mean scores at endpoint. 2. BDI mean scores at 6-month follow-up (interventions 1, 2 & 3 only). 3. Non-remitters (patients not acheiving status of being 'non-depressed' or | Country of study: US. Coping and supportive therapy were conducted by same two clinicians - advanced doctoral students in clinical psychology. | B |

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| | phase plus 6-month follow-up assessment in three intervention groups. Analysis: ITT - acute phase, completer - follow-up. | | enabling patients to cope with depression. 3. Supportive therapy: Emphasised supportive and modified person-centred techniques in a structured format. Therapist focused on maintaining and communicating empathy, congruence, and unconditional positive regard. Ten 2-hour sessions conducted each with a different goal. 4. WLC: Patients were informed that treatment would begin 11 weeks after initial assessment session. Patients were also given reassurance regarding prognosis and hope for improvement and informed that they would receive best approach available at start of treatment. At end of the study, coping treatment was given (data extracted for 11-week study period only). | BDI<=11) at endpoint. | | |

## Characteristics of excluded studies

| Study | Reason for exclusion |
|---|---|
| Blenkiron 2001 | Not an RCT. |
| Donnan 1990 | Patients did not have a primary diagnosis for depression. |
| Hannay 1999 | Study on GP's views on introducing therapeutic writing to patients in the practice. Not an RCT. |
| Holdsworth 1996 | Patients not diagnosed against recognised classification system. |
| Kiely 1986 | Sample did not consist of patients with depression, but consisted of those presenting with psychological problems in which stress played a part. |
| Robinson 1997 | No extractable data. |
| Sorby 1991 | Patients were diagnosed with DSM-III panic disorder. Only 12% patients diagnosed with DSM-III major depression, 8% with dysthymia. |

# Behaviour therapy (BT)

## Characteristics of included studies

| Study | Methods | Participants | Interventions | Outcomes | Notes |
|---|---|---|---|---|---|
| Dimidjian 2006 | Allocation: Random | Outpatients. N=241. Mean | 1. CBT. 2. Behavioural | 1. HRSD mean at endpoint | Therapists: CBT three licensed |

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| | (computer-generated list stratified by severity [HRSD <>20]). Duration: 16 weeks (24 sessions). | age: 40. Diagnosis: DSM-IV major depressive disorder. | activation. 3. Paroxetine (mean 35.17 mg) - plus CM. 4. Pill placebo plus CM (terminated at 8 weeks). | 2. Leaving the study. 3. Non-remitters (BDI <= 10). | psychologists with average 14 years' experience |
| Gallagher 1983 | Allocation: Random (no details). Duration: 12 weeks (16 sessions). | Outpatients referred from regional health centres or private physicians, or self-referred. N=30; 23 female. Age: 66-69. Diagnosis: RDC for major depressive episode. | 1. BT (using Lewinsohn manual 2. CT (using Beck manual | 1. Leaving the study early. | Mostly advanced PhD candidates in clinical psychology or post-doctoral clinical fellows. All experienced in the relevant therapy. Dropouts were replaced, and not clear if replacements were randomised. |
| Hopko 2003 | Allocation: Random (no details). Duration: 2 weeks (three times a week for 20 minutes). | Inpatients (token economy). N=25; 36% female. Mean age 30.5 years. Diagnosis: major depression (diagnosis method unclear). | 1. Behavioural activation + ADs. 2. Supportive psychotherapy + ADs. | 1. BDI mean at endpoint. | Master-level clinicians who had extensive training and experience with cognitive-behavioural interventions. Weekly supervision. |
| Jacobson 1996 | Allocation: Random (no details, but stratified). Duration: 2 weeks (three times a week for 20 minutes) + 6-month follow-up. | ?Primary care. N=152; 75% female. Mean age 37.5. Diagnosis: DSM-III-R major depression. | 1. Behavioural activation. 2. Automatic thoughts (data not extracted). 3. CBT. | 1. Leaving the study early. 2. HRSD mean at endpoint. 3. BDI mean at endpoint. | Four experienced cognitive therapists provided all three treatments. |
| McLean 1979 | Allocation: Random (no details). Duration: 10 weeks (between 8 and 12 sessions). | Outpatients. N=196; 72% female. Mean age: 39.2 (+-10.9). Diagnosis: Feighner criteria for clinical depression. | 1. Short-term psychotherapy. 2. Relaxation therapy. 3. BT. 4. Drug therapy (amitriptyline 75g up to 150mg [data not extracted]). | 1. Leaving the study early. | No description of therapists - all received pre-treatment training. NB: partners encouraged to attend treatment. Dropouts were replaced, and not clear if replacements were randomised. |

## Characteristics of excluded studies

| Study | Reason for exclusion. |
|---|---|
| Antonuccio 1984 | No control group. |
| Lichtenberg 1996 | Not randomised - participants assigned in cohorts. |
| McNamara 1986 | No evidence that depression diagnosis made according to recognised criteria. |
| Schulz 1999 | Not randomised. |
| Teri 1986 | 27% in concurrent treatment for depression. |

# Cognitive behavioural therapies (CBT)

## Characteristics of included studies

| Study | Methods | Participants | Interventions | Outcomes | Notes |
|---|---|---|---|---|---|
| Beach 1992 | Allocation: Random (no details). Duration: 15 weeks; 15-20 sessions. | Couples with marital difficulties recruited via press advertisements. N = 45 couples Diagnosis: women only - DSM-III for major depression or dysthymia. | 1. CT for female partner - following Beck *et a.l* (1979). 2. BMT. 3. Wait list - treatment on demand (3 hours crisis intervention if required) - no couples requested this. | 1. BDI mean endpoint scores. | CT and BMT - four therapists - were doctoral-level psychologists and two were advanced graduate students in clinical psychology. All had at least 4 years' full-time graduate training in clinical psychology. Also had 30 hours in each of the two treatments by nationally recognised experts before start of study. |
| Beutler 1991 | Allocation: Random (no details). Duration: 20 weeks; 3-month follow-up. | Outpatients, moderately depressed, recruited via press, word of mouth and professional recommendation. N=71. Mean age: 46.76. Diagnosis: DSM-III depression. | 1. Group CBT - following methods set out by Yost and Beck 2. Focused expressive psychotherapy - a Gestalt-based group psychotherapy supplemented by homework assignments. 3. Supportive self-directed therapy - weekly telephone contacts of 30 minutes each and reading prescribed books (data not extracted). Group size - 5–10 members. | 1. BDI mean endpoint scores. 2. HRSD mean endpoint scores. 3. HRSD mean scores at 3-month follow-up. 4. BDI mean scores at 3-month follow-up. | Therapists were four experienced psychologists trained in CT and focused expressive psychotherapy. Five advanced graduate students conducted supportive self-directed therapy. |
| Black-burn | Allocation: Random (no | Hospital outpatients (n=49) and GP | 1. CT - following Beck *et al.* (1979). | 1. Leaving the study | CT therapists - two of the authors |

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| 1981 | details). Duration: 20 weeks CT - twice a week for 3 weeks, then once a week. Follow-up study (Blackburn 1986). Duration: 24 months – 6-month continuation treatment (6-weekly appointments), 18 months naturalistic follow-up | patients (n=39). Diagnosis: RDC for major depression, BDI >= 14 follow-up: responders (50% increase in BDI scores) to Blackburn 1981. N = 41; 32 female. Mean age: 39.2 (+-12.2) to 47.9 (+-10.0) (reported by group). | 2. ADs (mixed - GPs and psychiatrists discussed range of ADs and dosages to be offered). 3. 1 + 2. Follow-up: 1. CT - 'booster' sessions every 6 weeks. 2. AD -maintained on same drug as in original study. 3. 1 and 2. | early. 2. Non-responders (<50% decrease in BDI). 3. Relapse (BDI > 9 and HRSD > 8) at 6, 12, 18 and 24 months. 4. HRSD mean scores after 6 months' maintenance. 5. BDI mean scores after 6 months' maintenance. | AD - GPs and psychiatrists. |
| Black-burn 1997 | Allocation: Random (according to stratified model [endogenous/non-endogenous, gender, age, number of episodes, severity]). Evaluators blind to treatment allocation. Duration: 16-week acute phase, 24-month continuation phase. CT - once per week during acute phase, maintenance phase - three times in first month, twice in second, monthly thereafter. AD - seen as outpatients roughly every 3 weeks for 30 minutes. | Outpatient referrals to consultants and from two general practices. N = 75*; 48 female. Mean age: 37.8 to 40.1 (reported by treatment group). Diagnosis: RDC primary major unipolar depression, HRSD >= 16, current episode was at least second major episode. *Total number in study, but only two of three treatment groups used (n=53). | Acute phase and maintenance phase treatments: 1. AD to AD - consultant or GP free to prescribe any AD provided equivalent to 100mg daily of amitriptyline for TCAs, 45 mg daily of phenelzine for MAOIs, or 20 mg daily of fluoxetine for SSRIs. During maintenance phase, had to be at least at recognised maintenance dose. 2. CT to CT - no details. 3. AD to CT - as above, but not clear if started CT at 'maintenance dose' (data not extracted for this comparison). | 1. BDI mean endpoint scores. 2. HRSD mean endpoint scores. 3. Non-remitters (HRSD - 17>6 or HRSD -24 >8 at endpoint). 4. Leaving the study early. 5. HRSD mean scores at 12- and 24-month follow-up. 6. BDI mean scores at 12- and 24-month follow-up. | Authors acted as CT therapists and had been 'extensively trained'. |
| Bright 1999 | Allocation: Random (blocked for gender and BDI, and then randomly assigned). Duration: 10 weeks, weekly 90- | Outpatients recruited via the press. N = 98; 70 female. Mean age 45.8. Diagnosis: DSM-III-R for major depression, dysthymia or | 1. Group CBT following Burns book Feeling Good. 2. Mutual support group therapy - focused on goals, like interpersonal insight, acquisition of | 1. BDI mean endpoint scores. 2. HSRD mean endpoint scores. 3. Leaving | Therapists were eight professionals and six para-professionals (data not extracted for paraprofessionals). |

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| | minute sessions. | depression not otherwise specified, HSRD>=10. | disclosure skills, sharing of advice and feedback.<br>Group size - seven members. | the study early.<br>4. BDI > 9.<br>5. HRSD > 11. | |
| Covi 1987 | Allocation: Random (no details).<br>Duration: 14 weeks, 15 2-hour group sessions. | Responders to press advertisements. N = 70 + 90 dropouts; 42 (out of 70) female. Mean age (of 70 subjects): 43.8.<br>Diagnosis: RDC diagnosis of major depression of at least 1-month duration, BDI >= 20, HRSD >= 14. | 1. Group CBT: followed Beck *et al.* (1979) and Covi *et al.* (1982). Prior to group, two 1-hour individual CBT sessions were conducted and a third after first two group sessions. At end of 14 weeks, non-improved patients received four additional individual CBT sessions.<br>2. Group CBT + imipramine.<br>3. Traditional group psychotherapy: based on inter-personal psychodynamic theories.<br>Group size: 6-8 members. | 1. BDI > 9.<br>2. Leaving the study early. | Therapists were a psychiatrist and psychologist who had received 2 years' training in CBT. Each therapist served as either main or co-therapist. |
| DeRu-beis 2005 | Allocation: Random (no details).<br>Duration: 16 weeks (20 sessions); continuation phase for treatment responders + 12-month naturalistic follow-up (three booster sessions) (not extracted). | Outpatients. N=240; 59% female. Mean age 40. | 1. CBT<br>2. AD paroxetine mean dose by week 16 37.3 mg (12.4 mg), plus CM (re-randomised to continuation AD or placebo in follow-up phase).<br>3. Pill placebo plus CM (not extracted - data available at 8 weeks only). | 1. HRSD mean at endpoint. | Six therapists: five licensed psychologists, one psychiatric nurse practitioner. |
| Dimid-jian2006 | Allocation: Random (computer-generated list stratified by severity [HRSD <>20]).<br>Duration: 16 weeks (24 sessions) | Outpatients. N=241. Mean age: 40.<br>Diagnosis: DSM-IV major depressive disorder. | 1. CBT.<br>2. Behavioural activation.<br>3. Paroxetine (mean 35.17 mg) - plus CM.<br>4. Pill placebo plus CM (terminated at 8 weeks). | 1. HRSD mean at endpoint.<br>2. Leaving the study.<br>3. Non-remitters (BDI <= 10). | Therapists: CBT three licensed psychologists with average 14 years' experience. |
| Elkin 1989 | Allocation: Random (no details). Duration: 16 weeks - CBT 12 sessions in first 8 weeks, then | Outpatients. N = 239. Age: 21-60.<br>Diagnosis: RDC criteria for definite major depression, HRSD >= 14 early | 1. CBT - following Beck *et al.* (1979).<br>2. IPT - aims to help patients achieve a better understanding of their interpersonal | 1. BDI mean endpoint scores.<br>2. HRSD mean endpoint | Therapists were a different group of experienced therapists for each condition, except for CM groups, |

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| | eight sessions once a week (20 sessions in total), IPT - 16 weekly sessions with optional four additional sessions at therapist discretion (all psychotherapy sessions 50 minutes); imipramine-CM and P-CM groups 16 weekly sessions with one or two additional tapering-off sessions, initial pharmacotherapy session 45-60 minutes, remaining sessions 20-30 minutes. | onset group defined as an episode of major depression beginning before age 21 and lasting > 2 years. | problems and to improve social functioning.<br>3. Imipramine-CM - flexible dosage schedule with general goal of achieving 200 mg/day by third week, may be increased to 300 mg/day. Administered within context of CM sessions, to provide supportive atmosphere and for psychiatrist to assess clinical status.<br>4. P-CM - as 3 but with pill placebo. | scores.<br>3. Leaving the study early.<br>4. Non-remitters (HRSD - 17>6 at endpoint).<br>5. BDI > 9 at endpoint. | which were carried out double blind by same therapists.<br>28 therapists (ten psychologists, 18 psychiatrists) all trained in pilot stage of project. |
| Fava 1994 | Allocation: Random (no details). Duration: ten 40-minute sessions every other week, plus follow-up at 2, 4 and 6 years | Outpatients N = 43; 26 female. Mean age: 43.7. Diagnosis: residual symptoms following major depression according to RDC with no evidence of depressed mood after successful treatment of between 3 and 5 months on Ads. | 1. CT - following Beck *et al.* (1979).<br>2. CM - monitoring medication tapering, reviewing clinical status, providing support and advice. | 1. Relapse rates at follow-up. | Same psychiatrist who was also an experienced therapist saw all patients. Integrity of treatment checked by random audio taping of four sessions in each group. Relapse = occurrence of RDC-defined episode of major depression. |
| Freeman 2002 | Allocation: Random (no details). Duration: 16 sessions | Primary care. N =100; 79 female. Mean age 36 (+-11.2). Diagnosis: major depression or depression with comorbid anxiety. | 1. IPT (no details).<br>2. CBT (no details).<br>3. TAU (no details ).<br>(1 v 2 extracted for this review; 1 v 3 in IPT review) | 1. HRSD mean scores at endpoint and 5-month follow-up.<br>2. BDI mean scores at endpoint and 5-month follow-up.<br>3. Leaving the study early. | 19 therapists (12 CBT and seven IPT - none did both) four clinical psychologists, five research psychologists, three psychiatrists, two nurse therapists, one OT, four CPNs. Data sub-set of larger study including wider range of depressive and anxiety disorders. |
| Gallag-her 1982 | Allocation: Random (no | Outpatients, referred from | 1. CT - following Beck *et al.* (1979). | 1. Leaving the study | Four therapists used in CT and |

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| | details, but stratified by age and severity of current episode). Duration: 12 weeks, 16 sessions in all. | regional health centres and private physicians, or self-referred. N = 30 + replacements for dropouts (see Outcomes); 23 female. Mean age reported by group: CT 68.3 (+-7.7), BT 66 (+-5.7), brief relational 69 (+-4.8). Diagnosis: RDC diagnosis of current definite episode or non-psychotic major depression, BDI > 17 and HRSD > 14. | 2. BT - following Lewinsohn manual<br>3. Brief relational/insight psychotherapy (data not extracted). | early. | brief relational and five in BT. Most advanced PhD candidates in clinical psychology or post-doctoral clinical fellows. All had training for therapy which they administered and were supervised by experts. |
| Gallagher-Thompson 1994 | Allocation: Random (no details). Duration: 16-20 sessions, twice a week for first 4 weeks, then once week for remainder of therapy (?c20 weeks). | Outpatients - caregivers recruited through referrals from healthcare professionals approached by letter. N = 66; 61 female. Mean age: 62 (+-9.7). Diagnosis: RDC definite or probable major depression (n=45), RDC minor depression (n=20) or intermittent depressive disorder (n=1) (mean baseline BDI 19.2). Cared for elderly relatives. | 1. CT following Beck) and Lewinsohn manuals<br>2. Brief psychodynamic therapy following Mann manual | 1. Still meeting RDC criteria for major/minor/ intermittent depression at endpoint and 3-month follow-up.<br>2. Leaving the study early. | 13 therapists, each saw at least one client. Four were skilled in both therapies, so treated clients in both conditions. Two had terminal masters degrees in social work, rest were PhD-level psychologists. All had at least 1 year of supervised experience doing psychotherapy with depressed elderly people. |
| Hautzinger (in-pats) | See Hautzinger 1996 This is data from inpatients - data for both groups not reported together. | | | | |
| Hautzinger 1996 | Allocation: Random (no details, but done independently of researchers). Duration: 8 weeks + 1 year follow-up. CBT - 24 sessions, 50-60 minutes long. AD - CM for 20 minutes a week. | Inpatients (in a psychiatric clinic) and outpatients. N = 191; 120 female. Mean age 38.8 (+-9.9). Diagnosis: ICD-9/DSM-III-R for major depression HRSD >= 20 BDI >= 20. 80.4% had major depression (DSM-III-R), | 1. CBT - following Lewinsohn (1974) and Beck et al (1979).<br>2. Amitriptyline - Week 1: 50-100mg/day Weeks 2-7: 150mg/day Week 8: stopped or continued depending on patient status + CM<br>3. 1 and 2 (without CM). | 1. BDI mean endpoint scores.<br>2. HRSD mean endpoint scores.<br>3. Leaving the study early.<br>4. HRSD mean scores at 12-month follow-up<br>5. BDI mean | Clinical psychologists and psychiatrists with at least 1 year clinical psychiatric experience. |

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| | | 19.6% dysthymia. | | scores at 12-month follow-up. | |
| Jarrett 1999 | Allocation: Random, blind to research personnel, supervised by statistician, stratified by length of current episode and marital status. Acute phase + continuation phase. Acute phase: duration: 10 weeks. CT = 20 sessions twice weekly. Pharmacolog-ical treatments: 11 sessions over 10 weeks. Continuation phase: 8 months' more treatment plus 16-month follow-up. CT - 10 sessions over 8 months. Pharmacother-apy: 10 sessions over 8 months. WLC - 10 sessions with evaluator over 8 months. | Outpatients, recruited through media, printed announcements, self- or practitioner referrals. Acute phase: N = 108; 73 female. Mean age: 39.6. Diagnosis: DSM-III-R for major depression, HRSD >= 14, definite atypical depression. Continuation phase: responders only, defined as HRSD < = 9, not meeting DSM-III-R for major depressive disorder at post-acute phase blind evaluation, completed acute phase treatment. N = 31; 26 female. Mean age: 41.2 (+-10.5). | Acute phase:<br>1. CT following Beck *et al.* (1979).<br>2. CM* + phenelzine - gradually increased over 10 weeks to 0.85mg/kg or 1mg/kg in patients not responding to lower dose.<br>3 CM* + placebo<br>* 2 and 3 - used treatment manual modelled on NIMH Treatment of Depression Collaborative Research Program - sessions involved adjusting medication, recording symptoms, side effects, weight, blood pressure. Not clear if included same support element as in Elkin1989. When symptom reduction and monoamine oxidase inhibition of 80% or more were achieved, patient continued to receive that dose. Compliance assessed by pill counts and patient diaries.<br>Continuation phase:<br>1. Acute phase CT + continuation CT.<br>2. Acute phase CT + no continuation treatment.<br>3. Acute phase phenelzine + continuation phenelzine (maintained on acute phase dose).<br>4. Acute phase phenelzine + no continuation treatment.<br>5. Acute phase placebo + continuation placebo.<br>6 Acute phase placebo + no continuation treatment. | 1. BDI mean endpoint scores.<br>2. HRSD-21 mean endpoint scores.<br>3. Leaving the study early.<br>4. Relapse at endpoint, 12-month and 24- month follow-up. | Therapists - two were doctoral-level clinical psychologists, one was a psychiatrist. Offsite consultant used Cognitive Therapy Scale to evaluate competence and provide feedback. Therapists participated in weekly group supervision. |
| Jarrett 2001 | Allocation: Random, using statistical software, double blind. Duration: 20 sessions over 12-14 weeks. | Outpatients recruited through media, announcements and referrals. N = 84; 61 female. Mean age: 42.74 (+-1.14). Diagnosis: | 1. CBT - following Jarrett unpublished manual designed to teach responders to prevent relapse.<br>2. Evaluation only. | 1. Leaving the study early. | Five experienced therapists provided CBT. Each had at least 1 year of training. Competence evaluated by off-site consultant. Therapists received |

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| | | responders (no major depressive disorder, HRSD <= 9) to acute phase where were diagnosed according to DSM-IV. | | | weekly supervision. |
| Keller 2000 | Allocation: Random, central computerised randomisation schedule. Assessors blind to treatment group. Duration: 12 weeks. Therapy group - twice-weekly sessions in weeks 1 to 4 (could be extended to week 8 if necessary), weekly weeks 5 to 12. AD group - 15-20 minutes per visit. Psychopharma-cologists not allowed to make formal psychotherapeu-tic interventions HRSD >=20. | Outpatients recruited from 12 academic centres. N = 681; 65.3% female. Mean age: 43 (+-10.7). Diagnosis: DSM-IV for chronic major depressive disorder, current major depressive disorder superimposed on pre-existing dysthymic disorder, recurrent major depressive disorder with incomplete remission between episodes in a patient with a current major depressive disorder. HRSD-24 >=20. | 1. Cognitive behavioural-analysis system of psychotherapy (draws on behavioural, cognitive, and interpersonal techniques of other therapies. Teaches patient to focus on consequences of behaviour and to use social problem-solving algorithm to address interpersonal difficulties. Differs from CBT by focusing primarily on interpersonal interactions). 2. Nefazodone + CM (following NIMH manual) - initially 200mg/day, then 300 mg/day in second week. Increased weekly in increments of 100mg/day to max of 600mg/day. To remain in study patients had to be on at least 300mg/day by week 3. 3. 1 and 2. | 1. Non-remitters (HRSD -17>6 or HRSD -24 >8). 2. Leaving the study early. 3. HRSD-24 mean endpoint scores. | Psychotherapists - minimum 2 years' experience after MD or PhD, or minimum 5 years' experience after Masters in Social Work. Also attended 2-day training workshop, with competence being evaluated during pilot cases. Dropout and remission data extracted on full ITT basis. HRSD at end of treatment reported as 'modified ITT' - i.e. only those who received at least one treatment session. |
| Klein 1984 | Allocation: Random (no details) Duration: 12, 2-hour, weekly sessions | Recruited via local newspaper. N = 74; 53 female. Mean age: 30. Diagnosis: Met RDC criteria for major or minor depression, not receiving any other treatment for depression, not displaying psychotic or bipolar disorder or imminent suicide risk. | 1. Group therapy (CBT/IPT). 2. Group meditation-relaxation therapy. 3. Running therapy (not extracted). | 1. Leaving the study early. | Dropout rates were the only extractable data. Four therapists - all conducted running therapy, two conducted meditation therapy as well, one of those and one other conducted group CT. All were mental health professionals. |
| Miller | Allocation: | Inpatients - | 1. Standard treatment: | 1. BDI mean | Pharmacotherapy |

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| 1989 | Random (no details) Duration: 3 weeks in hospital + 20 weeks post-hospital. Standard treatment: 20-minutes once per day in hospital, 6-8 times during outpatient period. CT: 50 minutes once per day in hospital (from third week), once per week as outpatient. Therapists could increase frequency if required. Social skills training: 50 minutes once per day in hospital (from third week), once per week as outpatient. Therapists could increase frequency if required. | recent admissions to private psychiatric hospital in US. N = 46; 34 female; 30 married. Age: 18-65. Diagnosis: major depression according to Diagnostic Interview Schedule BDI > 17 HRSD > 17. History of depression - mean no. of previous episodes 6.7. 44% also had dysthymia. | usual hospital milieu, medication (amitriptyline or desipramine) + other medication as considered appropriate, and management sessions with psychiatrist. 2. CT: standard treatment (as above) + CT as per Beck *et al.* manual (1976) 3. Social skills training: based on Bellack manual (data not extracted). | endpoint scores. 2. HRSD mean endpoint scores. 3. Leaving the study early. 4. BDI > 9 at endpoint. 5. Non-remitters (HRSD -17>6 or HRSD -24 >8). 6. HRSD > 6 at endpoint. | and maintenance conducted by seven board-certified psychiatrists. CT conducted by a PhD clinical psychologist with 6 years' experience of CT with depressed patients. Social skills training administered by post-internship clinical psychology PhD candidate with 12 years' experience, supervised by PhD clinical psychologist with 10 years' experience. |
| Miranda 2003 | Allocation: Random (computer generated); assessors blind to allocation. Duration: 6 months. CT = eight sessions (+ eight more if needed). | Women screened in Women, Infants and Children food subsidy programs targeting low-income pregnant and post-partum women or Title X family planning clinics for young and low-income women; all from three cultural groups (black women born in US n=117, Latinas born in Latin America n=134 and white | 1. CBT (eight weekly sessions + eight more if needed, n=15) - manual-guided treatment adapted from 12-sessions, patient and therapist manuals developed for low-income English and Spanish speaking medication patients. Shortened to eight sessions by including more topics per session and modified to be more sensitive to the issues of young women and those with histories of interpersonal trauma. Therapists also trained in PTSD and trauma. 2. Medication - paroxetine | 1. Mean HRSD endpoint scores. 2. Non-remitters (HRSD > 7). | Medication - treated by primary care nurse practitioners supervised by a board-certified psychiatrist; weekly telephone calls to assess adverse effects, adherence and treatment effects. CBT - treated by experienced psychotherapists supervised by licensed clinical psychologist with CBT expertise. Bilingual providers |

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| | | women born in US n=16. N = 267; all female. Mean age: 29.3 (+-7.9). Diagnosis: major depressive disorder (diagnosed by telephone interview). | 10mg-50mg (mean 30 mg) (n=18 switched to buproprion because of side effects) for 6 months. 3. Referral to community care - education about mental health treatments available in the community and about depression. Clinician offered to make an appointment for the women at the end of the clinical interview. Referred patients were contacted to encourage them to attend the intake appointment for care. All participants assigned to CBT or ADs invited to up to four education meetings with clinician overseeing their treatment. | | treated Spanish-speaking women and all written material was available in Spanish. |
| Murphy 1984 | Allocation: Random (according to pre-arranged system based on their unique and permanent clinic registration number). Only principal investigator knew assignment, and had no contact with patients except to draw occasional blood sample. Duration: 12 weeks, plus -1 month follow-up. CT - 50-minute sessions, twice weekly for first 8 weeks, then weekly for final 4 weeks. 1-, 6- and 12-month follow up. | Outpatients. N = 87 (one treatment group not extracted, therefore n=70). Characteristics available for completers only - 52 female, mean age: 33.8 (10.4). Diagnosis: primary, unipolar affective disorder (DSM-III), BDI >= 20, HRSD >=14. | 1. CT - following Beck *et al.* (1979). 2. Nortriptyline hydrochloride (equivalent to 25mg nortriptyline base). 3. CT + placebo (not extracted). 4. CT and TCA. | 1. BDI mean endpoint scores. 2. HRSD mean endpoint scores. 3. Relapse at 6 and 12 months. 4. Leaving the study early. 5. Non-remitters (HRSD -17>6 or HRSD -24 >8). 6. BDI > 9 at endpoint and 12 months. 7. HRSD mean scores at 1-month follow-up. 8. BDI mean scores at 1-month follow-up. 9. HRSD > 6 at endpoint. | Therapists were three psychologists and nine psychiatrists. Pharmacotherapy administered by the psychiatrists. Psychiatrists training ranged from second year residency to post residency. Psychologists had completed doctoral requirements except for dissertation. Therapists received pre-study training. |
| Murphy 1995 | Allocation: Random using table of random | Outpatients recruited via the press. N= 37 (one | 1. CBT - following Beck *et al.* (1979). 2. Relaxation training (not | 1. BDI > 9 at endpoint. | CBT therapists - three psychologists with at least 3 |

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| | numbers, concealed from patient until after randomisation. Duration: 16 weeks. Therapy sessions: 50 minutes, one or two times a week for first 4 weeks, then once per week, to max of 20. AD group - 20 minutes weekly for 4 weeks, then weekly or bi-weekly as appropriate. | treatment group not extracted, therefore, n=23); 26 female. Mean age: 39.4 (+-10.9). Diagnosis: DSM-III-R for unipolar affective disorder, depressed, BDI >= 14, HRSD > = 10. | extracted).<br>3. Desipramine - 150-300 mg daily. | | years' supervised clinical experience, given pre-treatment supervision and training, consisting of weekly supervision over period of several months Relaxation therapists: three psychologists and social worker. ADs administered by psychiatrist. |
| Paykel 1999 | Allocation: Random, consecutively numbered sealed envelopes prepared by statistician and stratified by centre, previous major depressive episodes (>=2 or <2), length of present illness (>=1 year and < 1 year), and severity of depression. Duration: 16 sessions over 20 weeks, booster sessions 6 and 13 weeks into 1-year follow-up. Drug continuation and CM continued for follow-up year. | Psychiatric outpatients with residual symptoms. N=158; 78 female. Mean age: control group 43.2 (+-11.2), CT group 43.5(+-9.8). Diagnosis: DSM-III-R for major depression within last 18 months with residual symptoms for at least 8 weeks at randomisation (HRSD >= 8, BDI >=9), and had to have been taking ADs for at least previous 8 weeks, with 4 weeks at equivalent to 125mg amitriptyline. Excluded if had CT of > 5 sessions previously. | 1. Drug continuation and CM: 30-minute session every 4 weeks with study psychiatrist for 20 weeks, then every 8 weeks. AD dosage allowed to increase by 30%.<br>2. Drug continuation and CM + CT: as above, plus 16 CT sessions over 20 weeks, plus two booster sessions at approximately week 26 and 32. Based on Beck *et al.* (1979) with a manual. | 1. BDI mean endpoint scores.<br>2. HRSD mean endpoint scores.<br>3. Leaving the study early.<br>5. Relapse at endpoint.<br>6. Relapse at follow-up.<br>7. HRSD mean scores at follow-up.<br>8. BDI mean scores at follow-up. | CT therapist trained and experienced in CT. regular joint supervision during study by principal author, plus independent rating of audiotapes. |
| Rosner 1999 | Allocation: Random (no details). Duration: 20 weeks, one | Outpatients. N = 76 (one treatment group not extracted, therefore n=43). | 1. CBT - following Beck *et al* (1979).<br>2. Gestalt therapy.<br>3. Bibliotherapy (data not extracted). | 1. BDI mean endpoint scores. | Psychologists or psychiatrists with 10 years' experience. |

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| | session per week. | Diagnosis: DMS-III for major depression HRSD >= 16. | | | |
| Scott 1992 | Allocation: Random using pre-prepared sealed envelopes. Duration: 16 weeks; CBT 50-minute sessions, weekly at start and then variable intervals. | Outpatients referred by 63 GPs in Edinburgh. N = 121 (data for two treatment groups not used, therefore n=61); 91 women. Mean age: between 28.8 (+-8.1) and 36.2 (+-14.2) (reported by treatment group). Diagnosis: DSM-III for major depressive episode. | 1. Usual GP care (19/29 included ADs, but only 14 at dose equivalent to therapeutic does of amitriptyline). 2. Amitriptyline prescribed by research psychiatrist - 50-75mg daily, gradually increasing to 150mg daily. Patients seen weekly for 2 weeks, then fortnightly/monthly as required. 3. CBT - based on *Beck et al.* 1979 4. Social work - detailed social assessment leading to construction of a problem list and thereafter an intervention programme. Initial sessions weekly but thereafter sessions were flexible. Strategies included support by encouragement and listening, help to understand feelings, practical advice, rehearsing events, support by the exercise of authority, advocacy on patient's behalf, arranging social support or holidays, marital/family meetings if appropriate. | 1. HRSD mean endpoint scores. 2. Leaving the study early. | CBT therapists - research clinical psychologists, trained in *Beck et al.* (1979) techniques. Social work - two qualified social workers, with experience of medical and psychiatric hospital patients. Assessments by independent trained raters who were initially blind to treatment group, but likely that patients made them aware of allocation at later meetings. |
| Scott 1997 | Allocation: Random (no details). Duration: 6 weeks, 30-minute weekly sessions. 12-month follow-up (data not extracted as > 50% dropout/lost to follow-up). | GP referrals. N = 48; 32 female. Mean age: 41(10.4). Diagnosis: DSM-III-R for major depression, BDI>=20 and depressive episode of < 2 years. 29 had previous episode. | 1. Usual GP care (all but one patient in each group prescribed ADs). 2. GP care + brief CT - including homework and schema-based therapy. | 1. BDI mean endpoint scores. 2. HRSD mean endpoint scores. 3. Leaving the study early. | No therapist details. |
| Selmi 1990 | Allocation: Random (no details). Duration: 6 | Recruited via the press. N = 36; 23 female. Mean age: 28.2 (4.58). | 1. Computerised-CBT - written by one of authors in MIIS-CONVERSE who was trained in CBT | 1. BDI mean endpoint scores. 2. BDI > 9 at | Therapist - advanced graduate student in clinical psychology with |

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| | weeks,six sessions. | Diagnosis: SCL-90-R >= 65th percentile for psychiatric outpatients (on 13-item depression scale), BDI >= 16 and current RDC diagnoses of major/ minor/ intermittent depressive disorder based on modified version of SADS. | (data not extracted).<br>2. CBT - used treatment manual following same procedures as computerised-CBT.<br>3. WLC - participants could call for an appointment if needed, but none did. | endpoint.<br>3. HRSD > 6 at endpoint. | same training in CBT as author of computer program. |
| Shapiro (Mild) | See Shapiro 1994. | Mild defined as BDI scores 16-20. | | See Shapiro 1994. | Data from mild, moderate and severe cases reported separately. |
| Shapiro (Mod) | See Shapiro 1994 | Moderate defined as BDI scores 21-26. | | See Shapiro 1994. | Data from mild, moderate and severe cases reported separately. |
| Shapiro 1994 | Allocation: Random (no details).<br>Duration: 8- and 16-week versions of therapies (16 week extracted for main comparisons). 1-hour weekly sessions.<br>Follow-up at 45 weeks after pre-screening - for 16-week therapy, equivalent to 15 weeks after end of treatment. | Outpatients, recruited from self-referrers responding to recommendations by occupational health personnel or responding to publicity materials distributed at the workplace or by GPs, or referred directly by GPs or mental health services. N = 117; 61 female.<br>Mean age: 40.5 (+-9.5).<br>Diagnosis: DSM-III for major depressive disorder. | 1. CBT - 'a multimodal method somewhat more behavioural in emphasis than Beck *et al.*, 1979.<br>2. Psychodynamic-IPT - based on Hobson's conversational model. | 1. BDI mean endpoint scores.<br>2. BDI mean scores at 6- and 12-month follow-up. | Five therapists - UK-trained clinical psychologists, two had post-qualification training in PI methods and trained the others. All had at least two training cases in each treatment x duration condition. Data for 8-week therapy conditions extracted for short-term therapy comparison only. Twnety-five participants on medication at beginning of study - not clear if still the case at the end. |
| Thomp-son 2001 | Allocation: Random (no details)<br>Duration: 3-4 months, 16-20 sessions in all treatment groups. First 4 | Outpatients who responded to media advertisements or referred by community physicians, mental health | 1. CT - following Beck *et al.* (1979), with modifications for older patients to facilitate learning - e.g. slower rates of presentation.<br>2. Desipramine - starting at 10mg, increased | 1. BDI mean endpoint scores.<br>2. HRSD mean endpoint scores.<br>3. Leaving | AD group - psychiatrists following NIHM-TDCRP protocol. CT - eight clinical psychologists with at least 1 year's experience with |

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| | weeks - two sessions per week, then one session per week.<br>AD group: 30-minute sessions. | organisations, and social service agencies. N = 100; 67 women. Mwan age: 66.8 (+-5.9). Diagnosis: major depression according to RDC on initial screening, HRSD >=14, BDI >= 16. | according to tolerance. Mean stable daily dose 90 +- 63 mg. Plus CM adapted from NIMH-TDCRP manual for older people, sessions to support patients.<br>3. 1 + 2 combined - AD and CT sessions usually conducted back-to-back. | the study early. | geriatric patients with psychiatric symptoms. |
| Ward 2000 | Allocation: Random (numbered sealed opaque envelopes, blocked and stratified by severity on BDI. Patients with strong preference could choose treatment or be randomised only between treatment groups [i.e. not GP care], but analysis undertaken for preference group, three-way randomisation and two-way randomisation separately).<br>Duration: 6-12 weekly 50-minute sessions - no control over when ended. | GP referrals. N = 464; 75% female. Mean age: 34.8 (12.2). Diagnosis: BDI >=14, 62% depression main diagnosis, others 'no overall psychiatric diagnosis' or 'behavioural difficulties'. | 1. Usual GP care (30% in counselling group, 27% of CBT group on ADs).<br>2. CBT - complied with manualised problem formulation and staged intervention approach (Greenberger & Padesky Mind over Mood)<br>3. Non-directive counselling - used non-directive approach outlined in a manual developed by authors based on Rogers.<br><br>2 used in review of CBT. | 1. BDI mean scores at endpoint and 12-month follow-up.<br>2. Leaving the study early. | Counsellors - accredited by BACP. CBT therapists were psychologists accredited by BABCP and registered with UK Council for Psychotherapy. Several problems with this trial: a) 27% of CBT group were also prescribed ADs by their GP (despite GPs being asked not to) and data not reported separately b) no control over when sessions were finished (minimum of 6, but up to 12 on offer if necessary). BDI etc scores taken at baseline, 4 months and 12 months, but only managed to get date of therapy completion from 87% in CBT group and of these, only 80 had finished at 4 months. No other information reported on when sessions finished (presumably all within 12 months). c) although inclusion criteria included BDI >= |

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## Characteristics of excluded studies

| Study | Reason for exclusion |
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| Barkham 1996 | (CBT v ?IPT) No usable data. |
| Beck 1985 (US) | (CBT v CBT + AD) Included patients with personality disorder. |
| Beutler 1987 | Benzodiazepine (BZD) v placebo (PBO) v (Group) G-CBT + PBO v G-CBT + BZD) Not an RCT |
| Bolton 2001 | (CBT v GP care) No extractable data - reports HADS not BDI or HRSD |
| Bowers 1990 | (CBT + AD v relaxation therapy + AD v AD) Inadequate randomisation |
| Chaudhry 1998 | (CBT + AD v CBT + PBO) Not an RCT |
| Comas-Diaz 1981 | (CBT v WLC) No evidence that depression diagnosis made according to recognised criteria |
| Dunn 1979 | ('CBT' v AD + support) Not CBT. |
| Dunner 1996 | (CBT v AD) All patients were diagnosed with dysthymia. |
| Fava 1998B | (CBT v well-being therapy) Mixture of primary diagnoses, including panic disorder and OCD. |
| Fleming 1980 | (G-CBT v G-BT v G-non-directive therapy) Inadequate randomisation. |
| Free 1991 | (G-CBT) Not an RCT. |
| Gendron 1996 | (G-CBT v support group) Patients not specifically depressed. |
| Gordon 1987 | (G-CBT v no treatment control) Participants not diagnosed according to recognised criteria. |
| Green 1985 | (Structured multimodal group therapy) Not an RCT. |
| Hellerstein 2001 | (CBT +AD v AD) All patients were diagnosed with dysthymia. |
| Hirschfeld 2002 | ('CBT' v AD) Not CBT and no relevant outcomes. |
| Hogg 1988 (US) | (G-CBT v G-IPT) 27% of participants had adjustment disorder. |
| Hollon 1992 | (CBT v AD v CBT + AD) Randomised, but dropouts replaced. |
| Jarrett 1998 | (CBT) Not an RCT. |
| Jong-Meyer 1996 | (CBT + AD v supportive therapy + AD) Irrelevant comparison in this review. |
| Lapointe 1980 | (G-CBT v G-assertive therapy v G-insight therapy) No extractable data. |
| Lenz 2000 | (CBT) Not an RCT. |
| Lewinsohn 1990 | Adolescents |
| Neimeyer (1984) | Unpublished, could not get trial report. |
| Macaskill 1996 | (AD v AD + rational emotive therapy) Participants includes those with co-existing psychiatric disorder. |
| Manning 1994 | (G-CBT + AD) Not an RCT. Patients not exclusively depressed. |
| Maynard 1993 | (G-CBT v 'support' group v control) Inclusion criteria did not include a formal diagnosis of depression. |
| McNamara 1986 | (CT v BT v CT + BT v counselling) No evidence that depression diagnosis made according to recognised criteria. |
| Meresman 1995 | (AD v G-CBT) Not an RCT. |
| Miller 1999 | Sub-set of participants in Miller 1989. Inadequate randomisation. |
| Moore 1997 | (CT v AD for residual depression) Study arms < 10 each and only study in comparison. |
| O'Leary 1990 | Means only given in graph, but cannot be accurately read. No standard deviations although could impute these from F ratios. |
| Pace 1993 | (CT v no treatment control) Diagnosis of depression not made according to recognised diagnostic system. |
| Peden 2000 | (G-CBT v no treatment control) Patients not exclusively depressed at start of study. |

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| Persons 1999 | (CT v CT + AD) Not an RCT. |
| Reynolds 1986 | Adolescents |
| Ross 1985 | (CBT v G-CBT v WLC/GP care) No usable data. No clear description of treatment. Randomisation procedure not clear |
| Rotzer 1985 | Unpublished, could not get trial report. |
| Rush 1977 | (CBT v AD) Medication tapered and discontinued in last 2 weeks of study unlike in other studies. |
| Rush 1981 | (G-CBT v individual CBT v individual CBT + AD) Not fully randomised. |
| Scogin 1987 | Not CBT. |
| Shapiro 1982 | (G-CBT v individual CBT) Most participants had adjustment disorder. |
| Shapiro 1987 | (CBT v relationship-oriented therapy) Not fully randomised; cross-over design. |
| Shaw 1977 | (CBT v WLC) Diagnosis of depression not made according to recognised diagnostic system. |
| Smit2006 | (CBT + psychoeducation vs TAU vs combination) CBT combined with psychoeducational intervention; treatment as usual included counselling. |
| Steffen 1998 | (CBT v psychodynamic) Data pooled from two studies which have not been published. No within-study data presented only between study, therefore can not use because randomisation not undertaken between studies. |
| Steuer 1984 | (G-CBT v G-psychodynamic) Patients not randomised to treatment groups. |
| Stravynski 1994 | (G-CBT v G-CBT + AD) Does not give Ns of each treatment group or numbers leaving the study early. Not clear what Ns are for mean HRSD/BDI scores at each time point. |
| Taylor 1977 | (CT v BT v CBT) Diagnosis of depression not made according to formal criteria. |
| Teasdale 1984 | (GP care v CBT) No usable data. |
| Thomas 1987 | (G-CBT v G-self-control therapy) Diagnosis of depression not made according to formal criteria. |
| Thompson 1987 | (CBT v psychodynamic) Not clear what patient numbers are used in table reporting outcome measures. Dropout data not fully reported. |
| Tschuschke 2000 | (G-'analytic' v G-psychodynamic) Not an RCT; irrelevant comparison for this review. |
| Warren 1988 | (G-CBT v WLC) Participants not diagnosed with depression according to accepted criteria at start of study. |
| Wierbicki 1987 | (G-CBT v individual CBT) Participants have atypical depression. |
| Wilson 1983 | (CT v BT) Randomised, but dropouts replaced. |
| Wilson 1990 | (G-CBT v individual supportive therapy) Compares group CBT with individual support therapy - comparison not usable in this review. |
| Wollersheim 1992 | (G-CBT v supportive therapy v bibliotherapy v WLC) Therapeutic intervention not CBT. |
| Zettle 1989 | (G-CBT v partial G-CBT) Participants not diagnosed according to recognised criteria. |
| Zimmer 1987 | Unpublished, could not get trial report. |

# Counselling

## Characteristics of included studies

| Study | Methods | Participants | Interventions | Outcomes | Notes |
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| Bedi 2000 | Allocation: Random (in blocks of four stratified by GP practice; randomisation schedule held centrally and allocation made by | Outpatients recruited via GP practices. N = 103 (in randomised part of trial); 77% female. Mean age: 37.8 (+- | 1. ADs - written protocol giving choice of three ADs which must be given at adequate dose and continued for 4-6 months after | 1. BDI mean scores at endpoint and 12-month follow-up. 2. RDC scores > 3 at endpoint and 12-month follow-up. | Counsellors had to have at least 2000 hours of supervised experience or already be attached to primary care |

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| | telephone). Duration: six sessions of counselling with outcome measures taken 8 weeks after entry and at 12-month follow-up | 11.5). Diagnosis: RDC for major depression diagnosed by GP. | response; GPs not obliged to follow this (no information on compliance). 2. Counselling. | | teams. Allowed to adopt any approach they thought suitable for their patient knowing that the patient was depressed. Could not calculate dropout rates as no clear criteria on which to base a definition in this study. |
| Simpson 2003 | Allocation: Random using random number tables. Duration: 6-12 therapy sessions; assessment at 6 and 12 months. | Primary care - nine GP practices. N= 145. Therapy: 85% women; mean age: 42; GP care: 75% women; mean age: 44. Entry criteria BDI >=14. Concurrent psychotropic medication: 32% therapy and 24% GP group were taking it at beginning of trial; 31% and 40% respectively took it between start of trial and 6-month assessment 40% and 38% respectively prescribed it between 6- and 12-month assessment. | 1. Counselling following psychodynamic Freudian model + usual GP care. 2. Usual GP care. | 1. BDI mean scores at 6 and 12 months. 2. BDI >= 14 at 6 and 12 months. .3 Leaving the study early (by 6 months). | Six counsellors who had worked in general practice for at least 6 years. BAC accredited, received regular supervision. Some sessions taped to check adherence to approach. |
| Ward 2000 | Allocation: Random (numbered sealed opaque envelopes, blocked and stratified by severity on BDI. Patients with strong preference could choose treatment or be randomised only between treatment groups [i.e. not GP care], | GP referrals. N = 464; 75% female. Mean age: 34.8 (12.2). Diagnosis: BDI >=14, 62% depression main diagnosis, others 'no overall psychiatric diagnosis' or 'behavioural difficulties'. | 1. Usual GP care (30% in counselling group, 27% of CBT group on ADs). 2. CBT - complied with manualised problem formulation and staged intervention approach (Greenberger & Padesky, 1995a, | 1. BDI mean scores at endpoint and 12-month follow-up. 2. Leaving the study early by 4 months and by 12 months. | Counsellors - accredited by BACP. CBT therapists were psychologists accredited by BABCP and registered with UK Council for Psychotherapy. Several problems with this trial: a) 27% of CBT group were also prescribed ADs by their GP (despite |

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| | but analysis undertaken for preference group, Three-way randomisation and two-way randomisation separately). Duration: 6-12 weekly 50-minute sessions - no control over when ended. | | 1995b). 3. Non-directive counselling - used non-directive approach outlined in a manual developed by authors based on Rogers 1950 book.<br><br>2 used in review of CBT. | | GPs being asked not to) and data not reported separately: no control over when sessions were finished (minimum of 6, but up to 12 on offer if necessary). BDI etc scores taken at baseline, 4 months and 12 months, but only managed to get date of therapy completion from 87% in CBT group; of these, only 80 had finished at 4 months. No other information reported on when sessions finished (presumably all within 12 months). c) although inclusion criteria included BDI >= 14, only 62% had main diagnosis of depression. |

## Characteristics of excluded studies

| Study | Reason for exclusion |
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| Bellamy 2000 | Participants suffering from 'psychological problems' and not diagnosed as depressed. |
| Friedli 1997 | Participants suffering from 'emotional difficulty' and not diagnosed as depressed. |
| Gordon 1998 | Not an RCT. |
| Hemmings 1997 | Includes participants with diagnoses other than depression. |
| Mittelman 1995 | Only 40% of participants depressed. Also, not randomised. |
| Vonk 1999 | Participants suffering from 'psychiatric disorder' but not diagnosed as depressed. |

# Interpersonal psychotherapy (IPT)

## Characteristics of included studies

| Study | Methods | Participants | Interventions | Outcomes | Notes | A C |
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| de Mello 2001 | Allocation: Random (stratified by | Participants referred to psychiatric | 1. IPT + moclobemide - IPT adapted to | 1. HRSD mean endpoint scores at 12 and 48 weeks. | Therapist was a psychiatrist with psychotherapy | A |

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| | gender and early or late onset). Duration: 48-weeks: IPT: 16 weekly sessions + 6 monthly booster sessions; AD: 8 months. | outpatient clinics and a teaching hospital. N = 35; female 28. Age range 20-60. Diagnosis: ICD-10 for dysthymia (N=32 had double depression). | dysthymia; focus on grief, role dispute, role transition, or interpersonal deficits. 2. Moclobemide + routine care - for 8 months; 150 mg during first week and 300 mg thereafter. During clinical consultations, patients received unstructured psychoeducation and clinical assessments. | 2. Leaving the study early for any reason (NB during whole study period). 3. Leaving the study early due to side effects ('medication intolerance'). | experience, training acquired by reading IPT material, attending an IPT course and contacts with IPT therapist. | |
| Elkin 1989 | Allocation: Random (no details). Duration: 16 weeks. CBT - 12 sessions in first 8 weeks, then eight sessions once a week (20 sessions in total), IPT - 16 weekly sessions with optional four additional sessions at therapist discretion (all psychotherapy sessions 50 minutes); imipramine-CM and P-CM groups 16 weekly sessions with one or two additional tapering-off sessions, initial pharmacotherapy session 45-60 minutes long, remaining sessions 20-30 minutes. | Outpatients. N = 239. Age: 21-60. Diagnosis: RDC criteria for definite major depression, HRSD >= 14. | 1. CBT-following Beck *et al.* (1979). 2. IPT - aims to help patients achieve a better understanding of their interpersonal problems and improve social functioning. 3. Imipramine-CM -flexible dose schedule with general goal of achieving 200mg/day by third week, may be increased to 300 mg/day. Administered within context of CM sessions, to provide supportive atmosphere and for psychiatrist to assess clinical status. 4. P-CM- as 3 but with pill placebo. | 1. BDI mean endpoint scores. 2. HRSD mean endpoint scores. 3. Leaving the study early. 4. HRSD>7. 5. BDI > 9. | Therapists were different group of experienced therapists for each condition, except for CM groups which were carried out double blind by same therapists. 28 therapists (ten psychologists, 18 psychiatrists) all trained in pilot stage of project. | B |
| Frank 1990 | Allocation: Random (patients and members of their treatment team blind to medication or | Patients in their third or more depression episode, with previous episode no more than 2.5 | All patients had received acute phase imipramine (150-300mg) and IPT (weekly for 12 weeks, then bi- | 1. Relapse (HRSD > 14 + Raskin > 6) at end of 3-year maintenance phase. | Therapists were social workers, psychologists or nurse clinicians with masters or PhD degrees who | B |

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| | placebo). Duration: approximately 20-week acute phase; 17-week continuation phase, then patients randomised to 3-year maintenance phase. | years before onset of present episode and minimum 10-week remission between two episodes. N = 128. Mean age: 40.2 (-+ 10.9). Diagnosis: RDC for unipolar depression, HRSD > 14, Raskin Severity of Depression > 6. Patients entering the maintenance phase had major depression, though 14.3% of patients entering the first-phase of treatment diagnosed with bipolar disorder. | weekly for 8 weeks, then monthly for additional 4 months; not clear how many sessions in maintenance phase). Entered maintenance trial if HRSD < 8 and Raskin score < 6 for 3 consecutive weeks. 1. IPT - following Klerman *et al.* (1984). Goal was to maintain the well-state by improving the quality of social and interpersonal functioning. 2. IPT-M + placebo. 3. IPT-M + active imipramine. 4. Medication clinic + placebo. 5. Medication clinic +imipramine. | 2. Leaving the study early (at end of 3-year maintenance phase). | were trained in IPT by two members who developed IPT and a certified IPT trainer. Data extracted for the following comparisons of interventions: 1 v 3 and 1 v 4. | |
| Freeman 2002 | Allocation: Random (no details). Duration: 16 sessions over 5 months, plus 5-month follow-up. | Primary care. N =124 (depressed or depressed with anxiety); 79 female. Mean age: 36 (+-11.2). Diagnosis: DSM-IV major depression or depression with comorbid anxiety. | 1. IPT (no details). 2. CBT (no details). 3. TAU (GP care, not controlled but GPs instructed not to refer to psychological therapy or counselling; all on ADs). (1 v 3 extracted for this review; 1 v 2 in CBT review.) | 1. BDI mean scores at endpoint and at 5-month follow-up. | 19 therapists (12 CBT and seven IPT - none did both). Four clinical psychologists, five research psychologists, three psychiatrists, two nurse therapists, one OT, four CPNs. Data sub-set of larger study including wider range of depressive and anxiety disorders. | B |
| Reynol-ds 1999 | Allocation: Random (stratified: by single/recurrent episodes of major depression); AD/placebo | Participants who responded to advertisements or letters sent from the investigators to surviving spouses identified | 1. Medication clinic + nortriptyline. 2. Medication clinic + placebo. 3. IPT + nortriptyline. | 1. Leaving the study early (acute phase). 2 .Non-remitters (by end of acute phase; HRSD not <7 for 3 | Therapists were experienced clinicians trained to and maintained at research levels of proficiency in IPT, same | C |

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| | administered double blind. Patients originally randomised to two-arm trial, but later addition of two further arms - results presented for four-arm trial, including patients originally randomised to two arms. Duration: Acute phase until patients remitted within an 8-week period, patients who remitted entered into a 16-week continuation phase and followed-up after 2 years; IPT - weekly 50 minute sessions. | in obituaries. N = 80; 68 female. Mean age: 66.4. Diagnosis: SDAS-L and RDC for major depressive episode. | 4. IPT + placebo. | consecutive weeks). 2. Relapse (patients in continuation phase only). 3. Leaving the study early due to side effects (acute phase). | clinicians also provided the medication clinic. | |
| Reynolds 1999B | Allocation: Random (schedule generated by project statistician, individual randomisation stratified by therapist and blocked in units of four subjects, patients and therapists blind to AD or placebo assignment). Duration: Initial acute treatment phase - received nortriptyline + weekly IPT to achieve remission, 16-week continuation treatment phase - nortriptyline + fortnightly IPT. Patients showing | Older adults in at least their second lifetime episode and previous episode no more than 3 years before present episode. N = 107. Age: 69 between 60 & 69 years, 38 > 69.Diagnosis: RDC for unipolar major depression, HRSD >16. | 1. Nortriptyline + IPT. 2. Nortriptyline + medication clinic. 3. IPT + placebo. 4. Medication clinic + placebo. | 1. Leaving the study early (at end of 3-year maintenance phase - included patients who refused treatment and medical dropouts). 2. Relapse (at end of maintenance phase). | Therapists were experienced clinicians trained to research level of proficiency by four of the investigators. Same clinicians also provided medication-CM to medication clinic group. Recurrence of major depressive episode based on structured psychiatric interview. | A |

| | | | | | | |
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| | stable remission then randomised to one of four 3-year maintenance therapy conditions; IPT - monthly 50-minute sessions, medication clinic - monthly 30-minute visits. | | | | | |
| Schulb-erg 1996 | Allocation: Random (no details). Duration: 8 months. IPT: acute phase 4 months (16 weekly sessions); continuation phase: 4 months (4 monthly sessions); AD: acute phase 6 weeks, 6-month continuation phase. | Primary care patients presenting at study site waiting rooms in four ambulatory health centres. N = 276; 229 female. Mean age: 38.1. Diagnosis: for entry to acute phase: DSM-III-R for major depression, HRSD > 12; for continuation phase (AD group only): BDI < 20 and judged to be non-responder by independent psychiatrist. | 1. IPT – Klerman *et al.* (1984). 2. Nortriptyline + CM 3. TAU - usual family physician care; 45% prescribed ADs within 2 months of randomisation. | 1. HRSD mean scores at endpoint (month 4 data) and after 4 months' continuation treatment (month 8 data). 2. Leaving the study early. 3. HRSD >7 after 4 months' continuation treatment (month 8 data). | Therapists were psychiatrists and clinical psychologists skilled in psychotherapeutic procedures trained in standardised IPT. | B |
| Weiss-man 1992 | Allocation: Random (double-blind to ADs or placebo). Duration: 6 weeks, weekly 30-50 minute IPT sessions. | Outpatients, ambulatory. N = 35; 25 female. Mean age: 70 (range 60-83 years). Diagnosis: DSM-III major depression. | 1. IPT + alprazolam (mean maximum dose 2.2mg). 2. IPT + imipramine (mean maximum dose 97.5mg). 3. IPT + placebo. 1 not extracted . | 1. Leaving the study early for any reason. 2. Leaving the study early due to side effects. | IPT was offered for ethical reasons in light of the placebo and to enhance compliance in general. Evaluating the efficacy of IPT as such was not the objective. IPT based on Klerman *et al.* (1979) | B |

## Characteristics of excluded studies

| Study | Reason for exclusion |
|---|---|
| DiMascio 1979 | > 50% dropout rate (53/96); also, efficacy data not extractable because no SDs. |
| Frank 1989 | No extractable data. |
| Jacobson 1977 | Raskin Depression Scale used for depression diagnosis. |

| | |
|---|---|
| Klerman 1974 | No extractable data. |
| Martin 2001 | Four out of 15 patients in venlafaxine group and one out of 13 patients in the IPT group was assigned in a non-randomised manner. |
| Mossey 1996 | Patients with "subdysthymia"- a sub-threshold level for major depression or dysthymia. Excluded patients with major depression or dysthymia. |
| Szapocznik 1982 | Not an RCT; formal diagnosis of depression not conducted. |
| Zeiss 1979 | Patients recruited based on MMPI. |

## Problem solving therapy (PST)

### Characteristics of included studies

| Study | Methods | Participants | Interventions | Outcomes | Notes | A C |
|---|---|---|---|---|---|---|
| Dow-rick 2000 | Allocation: Random using random number tables. Nine-centre study with all but one centre offering one of two treatments and no-treatment control. Therefore, comparisons can be made only between each treatment and relevant control, not between two treatments. Duration: Six sessions (total time < 4hours). | Recruited from GPs. N = 426 identified via a survey; 277 female. Age: 18-65.Diagnosis: 52% single major depressive disorder, 19% recurrent major depressive disorder, 16% dysthymia, 4% adjustment disorders, 9% other; BDI at baseline - PST group: 23.11 (7.65), Control group: 22.51 (8.01) | 1. PST. 2. Group psychoeducation (not extracted). 3. No treatment control. | 1. Number diagnosed with depressive disorder at 6 and 12 months. | | |
| Myn-ors-Wall-is 1995 | Allocation: Random using sealed envelopes, stratified by severity of disorder. Duration: Six 30-minute sessions over 3 months. | Recruited from GPs. N = 91; 70 female. Mean age: 37. Diagnosis: RDC criteria for major depression, HRSD > 13. | 1. PST 2. Amitriptyline 150mg/day. 3. Placebo. | 1. Leaving the study early for any reason (based on number of participants not achieving six sessions). 2. HRSD mean endpoint scores. 3. BDI mean endpoint scores. 4. Leaving the study early due to side effects. 5. BDI > 8. 6. HRSD >7. | Therapists were one psychiatrist experienced in PST and two GPs who received training. Continuous data extracted for all patients completing at least four sessions. | A |
| Myn-ors- | Allocation: Random using | Referrals from GPs. N=151; | 1. PST/ GP. 2. PST / practice | 1. HRSD mean scores at endpoint and 1 year | Therapists were three | A |

| | | | | | | |
|---|---|---|---|---|---|---|
| Wal-lis 2000 | sealed envelopes, generated using list of random numbers, stratified for severity. Duration: Six fortnightly sessions, plus 1-year follow-up (from start of study). | 116 female. Mean age: 35. Diagnosis: Probable or definite major depression on research diagnostic criteria. HRSD > 13. Minimum 4 weeks' illness. | nurse. 3. AD - Fluvoxamine (n=7*, 100-150 mg) or paroxetine (n=64*, 10-40mg (most at 20mg). 4. PST sessions with nurse + AD. (1 and 2 added together for dichotomous outcomes; 1 entered for continuous outcomes) * n for AD alone and in combination | follow-up. 2. BDI mean endpoint scores at endpoint and 1-year follow-up. 3. Leaving the study early for any reason. 4. Leaving the study early due to side effects. 5. HRSD > 7 at endpoint and 1-year follow-up. | research GPs and two research practice nurses. All followed a treatment manual and had supervision from an experienced PS therapist who was also the author. | |

## Characteristics of excluded studies

| Study | Reason for exclusion |
|---|---|
| Alexopoulos 2003 | Participants with executive dysfunction. |
| Catalan 1991 | Patients not necessarily depressed. |
| Dowrick 2000 | Patients not all depressed. Some with adjustment disorder. |
| Garland 2000 | Not an RCT. |
| Lynch 1997 | Not clear what treatment was received by comparison group; dropout figures for comparison group not clear; BDI data from < 50% treatment group; SDs for HRSD scores not calculable. |
| Shipley 1973 | Not randomised. |
| Simons 2001 | Preliminary report - no results given. |
| Unutzer 2001 | Not all participants in treatment group received PST; also, no extractable outcomes. |
| Williams 2000 | Participants have diagnosis of dysthymia or minor depression. |
| Wood 1997 | Participants do not have primary diagnosis of depression. |

# Short-term psychodynamic psychotherapy

## Characteristics of included studies

| Study | Methods | Participants | Interventions | Outcomes | Notes | A C |
|---|---|---|---|---|---|---|
| Burnand 2002 | Allocation: Random (no details expect stratified by presence of personality disorder, previous episodes, gender). Duration: 10 weeks. | Outpatients referred for acute outpatient treatment at a community mental health centre. N = 95; 45 female. Mean age: 36. Diagnosis: DSM-IV major depressive disorder and HRSD >= 20 (mean baseline: | 1. Psycho-dynamic psychotherapy + clomipramine (dose as below). 2. Clomipramine 125 mg by day 6 (switched to 20-40mg citalopram in cases of bad side effects n=6) + supportive therapy (individual sessions aimed at | 1. Leaving the study early for any reason. 2. HRSD at endpoint (completers only). 3. Non-remitters (HRSD > 7) (from personal communication with authors). | Nursing teams were trained for 6 months in the use of specific manuals - those providing psychotherapy (n=4) had experience in crisis intervention practice under psychodynamic supervisions (>2 years) and received weekly | B |

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|---|---|---|---|---|---|---|
| | | combination 24.3 [+-3.2]; AD only 24 [+-2.9]). | providing empathetic listening, guidance, support and facilitation of an alliance by one carefully designated caregiver). | | supervisions with a psychoanalyst. | |
| Gallagher-Thompson 1994 | Allocation: Random (no details). Duration: 16-20 sessions, twice a week for first 4 weeks, then once a week for remainder of therapy (?c20 weeks). | Outpatients - caregivers recruited through referrals from healthcare professionals approached by letter. N = 66; 61 female. Mean age: 62 (+-9.7). Diagnosis: RDC definite or probable major depression (n=45), RDC minor depression (n=20) or intermittent depressive disorder (n=1) (mean baseline BDI 19.2 [+-]). Cared for elderly relatives. | 1. CT following Beck *et al.* (1979) and Lewinsohn *et al.* (1985). 2. Brief psychodynamic therapy (Mann, 1973). | 1. Still meeting RDC criteria for major/minor/intermittent depression at endpoint and at 3-month follow-up. 2. Leaving the study early. | 13 therapists, each saw at least one client. Four were skilled in both therapies, so treated clients in both conditions. Two had terminal masters degrees in social work, rest were PhD-level psychologists. All had at least 1 year of supervised experience doing psychotherapy with depressed elderly people. 1 and 2 not extracted: means/SDs presented by short-term or long-term carer, but not possible to discover 'n' used. | B |
| McLean 1979 | Allocation: Random (no details). Duration: 10 weeks, weekly 1-hour sessions. | Outpatients recruited through a three-stage screening process: telephone, clinical interview and psychometric evaluation. N = 154; out of initial 196 recruited, 141 female. Mean age: 39.2 (+-10.9). Diagnosis: Feighner *et al.* (1972), MMPI >=25 for men, >=29.5 for women; BDI >=23; Lubin's Depression | 1. Short-term psychotherapy - following Marmor manual goals were development of insight through psychodynamic forces that initiated the current depression 2. BT - helped clients to avoid their negative and introspective cognitive habits. 3. Amitriptyline started at 75 mg raised to 150mg,weaned at the rate of | 1. Leaving the study early . | Seven female and seven male therapists - licensed psychologists, physicians, or psychiatrists. Efficacy data not extracted since post-treatment sample included replacers. | B |

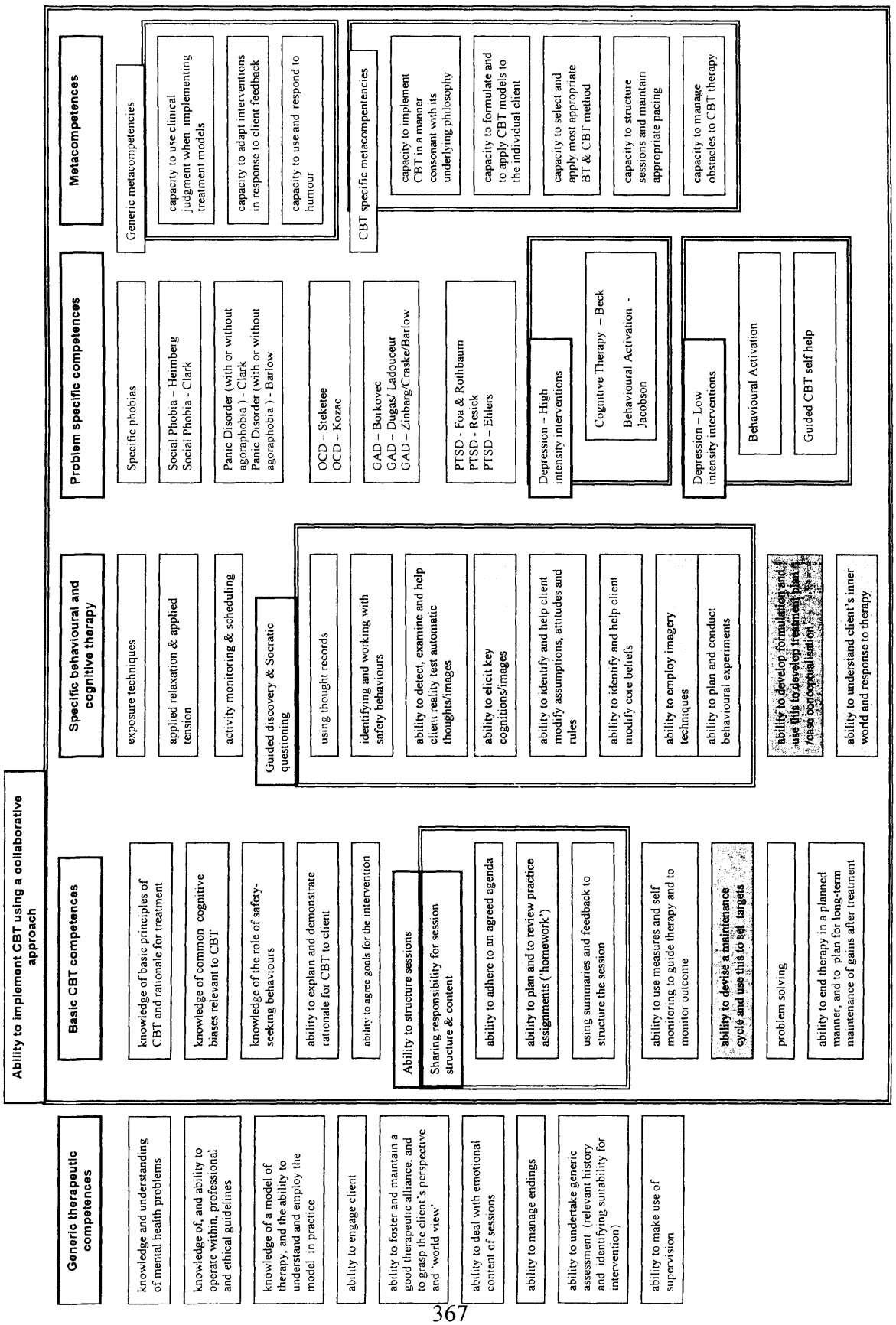
| | | | | | | |
|---|---|---|---|---|---|---|
| | | Adjective Check List >=14. | 25mg/day. 4. Relaxation therapy - goals were to appreciate the relation between muscle tension and depression and to return to his or her level of pre-episode physical functioning by developing a significantly increased ability to relax tension in all muscle groups (data not extracted). | | | |
| Shapiro (Mild) | See Shapiro 1994. | Mild defined as BDI scores 16-20. | | See Shapiro 1994. | Data from mild, moderate and severe cases reported separately. | B |
| Shapiro (Mod) | See Shapiro 1994 | Moderate defined as BDI scores 21-26. | | See Shapiro 1994. | Data from mild, moderate and severe cases reported separately. | |
| Shapiro 1994 (UK) | Allocation: Random; Duration: 8- and 16-week versions of therapies (only 16 week extracted). 1-hour weekly sessions. Follow-up at 45 weeks after pre-screening - for 16-week therapy, equivalent to 15 weeks after end of treatment. | Outpatients, recruited from self-referrers responding to recommendations by occupational health personnel or responding to publicity materials distributed at the workplace or by GPs, or referred directly by GPs or mental health services. N = 117; 61 female. Mean age: 40.5 (+-9.5). Diagnosis: DSM-III for major depressive disorder. | 1. CBT - 'a multimodal method somewhat more behavioural in emphasis than Beck *et al.*, 1979) 2. Psycho-dynamic-interpersonal psychotherapy - based on Hobson's conversational model. | 1. BDI mean scores endpoint, 6- month and 12-month follow-up. | Five therapists - UK-trained clinical psychologists, two had post qualification training in psycho-dynamic-interpersonal psychotherapy method and trained the others. All had at least two training cases in each treatment x duration conditions. Only data for 16-week therapy conditions extracted as most comparable with other studies. 25 participants on medication at beginning of | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | study - not clear if still the case at the end. | |

## Appendix K Membership of Expert Reference Group

| | |
|---|---|
| Professor Philippa Garrety (Chair) | Kings College London and South London and Maudsley Trust |
| Professor Ian Baguley | University of Lincoln |
| Dr Gillian Butler | Oxford Cognitive Therapy Centre |
| Professor David Clark | Institute of Psychiatry |
| Dr Amanda Cole | Chair of the Accreditation and Registration Sub-Committee of the BABCP |
| Professor Anke Ehlers | Institute of Psychiatry |
| Professor Mark Freeston | University of Newcastle |
| Professor Glyn Lewis | University of Bristol |
| Dr Christopher Mace | Royal College of Psychiatrists |
| Dr David Mathews | Skills for Health |
| Dr Freda McManus | Oxford Cognitive Therapy Centre |
| Professor Dave Richards | University of York |
| Dr David Veale | Institute of Psychiatry and South London and Maudsley Trust |
| Dr Dave Westbrook | Oxford Cognitive Therapy Centre |
| Dr Chris Williams | University of Glasgow |

# Appendix L Map of Competences



## Appendix M Local Depression Protocol

Camden and Islington Depression Guideline

**Key aims of depression guidelines:**

- To improve the recognition & recording of depression in primary care
- To promote assessment of risk and suicide prevention
- To promote primary care strategies for the management of depression
- To improve the drug management of depression
- To provide evidence-based guidance on referral for psychological therapies
- To advise on criteria for referral to specialist services

**Recognising depression**

***Background facts***

- Depression is a common disorder - it affects between 5-10% of people in the UK, and is the second most common cause of disability worldwide.
- The majority of people experiencing a depressive disorder will present to their GP, but will not necessarily overtly complain of psychological symptoms.
- In an average surgery session a quarter to a third of the patients will have symptoms of depression, and one new case will present per surgery. It is the third most common reason for consultation.
- Depression is the most common chronic disease, with rates exceeding asthma, diabetes and hypertension.
- Depression results in considerable emotional, physical and financial costs to the patient, their family and society. Effective identification and management of depression can improve outcomes both at an individual and societal level.
- Depression often involves a mixture of physical, psychological and social factors and so benefits from an assessment and management approach that takes into account these multiple factors.

- Depression varies in its level of severity and different management approaches are recommended dependent on severity.

Whilst the majority of people with a depressive illness will present in primary care at some point, a variety of factors mean that many may not mention their depressive symptoms directly.

**Reasons for not mentioning depression:**

- To avoid stigma & concerns about being diagnosed with a mental illness, and the feared potential effects of this on work, family and friends.
- Feelings of embarrassment or guilt at being unable to control feelings or "shake themselves out of it".
- Somatisation – patients may be very aware of their physical symptoms but find it hard to articulate the emotional experiences. In some cultures, the expression of physical symptoms is more acceptable. This may also be true of the medical culture! Also patients may not believe that a medical doctor will be interested in hearing about emotional issues and may find it hard to express their feelings.
- Concerns about antidepressants e.g. fears of addiction.
- Men are also less likely to talk about their emotional state than women.

It is therefore very important for primary care professionals to be on the lookout for depression amongst their patients, and to ask directly about it when low mood is suspected.

Depression can affect us all, but certain groups of people are at increased risk of depression, and so it will be important to be especially vigilant with these groups. It is also known that depression is often under-recognised and/or under-treated in some groups e.g. older people, or those from minority ethnic groups, children and adolescents.

**Higher Risk Groups**

- Past history of depression
- Family history of depression
- Women up to 6 months post-childbirth & women with young children
- Socially isolated
- Those with ongoing difficult relationships including domestic violence
- Concurrent physical illness, particularly chronic illness
- Multiple adverse events e.g. loss, bereavement, childhood separation or abuse
- Drug & alcohol misusers
- Carers
- Those in residential care

***Diagnosis of depression***

Although there are formal criteria for the diagnosis of depression (see below), it is important to remember that patients in primary care may not present directly with these commonly recognised symptoms. Depression should always be considered in patients presenting with the following:

- feeling "tired all the time"
- with pain that is non-specific, widespread or seems out of proportion to the physical cause
- other physical symptoms that are not explained by disease
- frequent attendance
- self-neglect.

In addition to asking about depression when clinically indicated by the patient's presentation is recommended that asking about someone's mental health is undertaken routinely in primary care at the following key times:

**Key times to routinely ask about a patient's mental health:**

At the **NEW PATIENT REGISTRATION CHECK** – by either the GP or Practice Nurse

At **POSTNATAL CHECKS** – screening for depression should be routinely carried out by Health Visitors/other Community Nurses in Camden & Islington, but GPs and Practice Nurses can also informally ask about new mother's emotional well-being at the six-week check or at child immunisation appointments.

**At OVER-75 HEALTH CHECKS** - by Practice Nurse or District Nurse

**Diagnosis of depression (using ICD-10 classification)**

A diagnosis of depression is indicated by the presence of at least two of the following core symptoms, plus some of the following additional symptoms, most of the day for at least two weeks.

**Core Symptoms (at least 2 of the following)**

- depressed mood, *and/or*
- loss of interest, *and/or*
- loss of energy & fatigue

**Additional Symptoms (plus some of the following)**

- poor concentration
- reduced self-esteem & self-confidence
- disturbed sleep
- change in appetite or weight
- feelings of guilt or worthlessness
- agitation/slowing
- pessimism/ hopelessness
- suicidal thoughts or acts

***Most of the day for at least 2 weeks***

As well as diagnosing depression it is also important to make an assessment of its severity as this will guide clinical decision-making in management. Differentiation between mild, moderate and severe depression relies on a complicated clinical judgement that involves the number, type and severity of symptoms present. The following diagnostic guidelines will be useful in that assessment.

**Assessing the severity of depression (ICD-10)**

**Mild depression**

Presence of at least two core symptoms plus at least two additional symptoms

- None of the symptoms should be present to an intense degree.
- The individual is usually distressed by symptoms, has some difficulty with ordinary work & social activities, but will not cease to function completely.

**Moderate depression**

Presence of at least two core symptoms plus at least 3 (preferably 4) additional symptoms

- Several symptoms likely to be present to a marked degree.
- The individual will usually have considerable difficulty continuing with social, work or domestic activities.

**Severe depression**

Presence of all three core symptoms plus at least four other additional symptoms

- Some symptoms should be of severe intensity.
- It is very unlikely that the individual will be able to continue with social, work or domestic activities except to a very limited extent.
- The individual usually shows considerable distress or agitation unless retardation is a marked feature.
- Loss of self-esteem or feelings of uselessness or guilt are likely to be present, and suicide is a distinct risk (see risk assessment).

**Dysthymia**

Presence of symptoms of mild depression (see above) for at least two years.

**Differential diagnosis**

When trying to make a diagnosis of depression it is also important to consider the following:

- **Acute adjustment disorders:** patients may present with an adjustment disorder in response to a recent life event. Although immediate support may need to be put in place, such disorders are generally short-lived and do not usually require pharmacological treatment.
- **Mixed anxiety and depression:** this is very common in primary care, so look out for symptoms of nervousness, panic or generalised anxiety. Where the depression is significant treat the depression using the treatment guidelines below and manage both the anxiety and depression symptomatically – see guidelines for management of anxiety.

- **Bipolar disorder:** this should be considered if there is a history of manic episodes (elevated mood, increased energy and an increase in the quantity and speed of physical and mental activity). Arrange a psychiatric assessment.
- **Substance misuse:** check alcohol and drug use as these often co-exist with depression. Depression can be a symptom of the substance misuse itself, or the patient may be using substances in an attempt to cope with depressive symptoms. Consider referral onto appropriate Drug or Alcohol Services in Camden & Islington. **(See Camden & Islington PCT's Alcohol Resource Manual or www.cimh.info for further details)**
- **Physical illness:** some physical conditions, such as hypothyroidism and anaemia, may mimic depression and should be considered and investigated where appropriate.
- **Iatrogenic causes:** some drugs may give rise to depressive symptoms – e.g. anti-hypertensives, oral corticosteroids, indomethacin and opiates.

**Good Practice Point 1**

> When a diagnosis of depression is made it should be recorded in the patients notes and/or on your practices electronic patient record using the appropriate Read Code. This will aid both individual patient management and allow practice audit and monitoring of mental health problems.

*Assessment of risk*

Risk of self-harm or suicide and risk to others should be considered in all patients presenting with depression.

- 70% of people who commit suicide are depressed.
- Although rare, consider risk of harm to others through aggression and & violence.
- Consider risk to self or others through neglect. Remember that risk can be subtle – are children being neglected or deprived because of parental depression? Are children or others having to play the role of carer and is this a risk to their own mental health?

See Risk Assessment Guideline for further information on questions to ask to assess risk.

**Good Practice Point 2**

> All patients presenting with depression should be asked about risk of suicide and self-harm and this recorded in the paper or electronic patient records (see depression template).

*Management of depression*

The available evidence suggests that choice of intervention(s) in depression should be largely determined by the severity of the patient's symptoms. However, in clinical practice, patient choice and clinical judgement will also be important factors in deciding treatment options. *All treatment plans should be developed in active collaboration with the patient, and could involve consultation with other family members/ carers where appropriate.*

As depression is generally a multi-factorial illness it is important to consider physical, psychological and social aspects of management. In this guideline strategies for management have been categorised as:

- Primary care management – non-drug interventions that you can provide as a primary care practitioner as part of your normal consultation.
- Pharmacological management – drug interventions.
- Psychological management – "talking therapy" interventions provided by mental health specialists either attached to the practice, or as part of local statutory or voluntary sector services (i.e. counsellors, clinical psychologists, psychotherapists).
- Referral on to specialist secondary care mental health services (psychiatrists, Community Mental Health Teams, Crisis Response Teams).

**Primary care management**

All patients with depression and other mental health problems can benefit from listening to their problems as part of the routine consultation, and the value of empathic support from a primary care practitioner should not be underestimated.

All primary care practitioners (GPs, Practice Nurses, Health Visitors, District Nurses and Community Midwives) can also help patients by doing the following:

Give information, advice and education about depression. Simple explanations about depression can help the patient make sense of their distressing symptoms and instil hope about recovery. It can also be helpful to give the patient and/or their family an information leaflet about depression to take away from the consultation to read later. The key messages to the patient and their family are that:

- depression is common
- effective treatments are available
- depression is an illness, not weakness or laziness
- can be part of a normal adjustment reaction e.g. bereavement

**Patient Information Leaflets**

The Health Promotion Library in Camden & Islington is able to provide your practice with copies of the following recommended leaflets which patients may find helpful:

| | |
|---|---|
| Understanding Depression | published by MIND |
| Understanding Anxiety | published by MIND |
| How to Cope as a Carer | published by MIND |

Alternative patient leaflet "Depression: An Information Leaflet" is included in the Resource Pack accompanying these guidelines. Further copies of these leaflets are available in the EMIS/Mentor Patient Information Leaflet directory or on the Northumberland Health Action Zone website www.northumberland-haz.org.uk/selfhelp

Offer **simple counselling, advice and problem solving** within the consultation around practical and social problems. Specific advice might be to:

- Plan short-term activities that give enjoyment or build confidence
- Resume activities that have been helpful or enjoyable in the past
- Resist pessimism & self-criticism and do not concentrate on negative or guilty thoughts
- Where there are significant social or welfare problems that the patient is unable to deal with independently, consider referral for Welfare Rights Advice
- Encourage the patient to make use of their existing relationships and social support structures
- Inform the patient of other voluntary sector agencies that might be of help to them. You can provide them with the Patient Information Sheet included with this pack.(not in amended should it come out?

**Welfare Rights Advice**

**Camden:** There are 3 Camden: there are 3 Citizens Advice Bureau offices in Camden, in Holborn, Kentish Town and Kilburn. Patients can ring directly on **08450 505152** to arrange an appointment. Primary care staff may wish to contact the offices directly for some patients, to facilitate access. (For contact numbers see practice contact sheet.)

**North Islington:** the Citizens Advice Bureau provides advice sessions at 4 surgeries in the area that any patients from practices in the North Islington area may access. Patients wishing to make an appointment at any of these surgeries should call: 020 7561 7455

**South Islington:** Islington People's Rights provides advice sessions in 10 surgeries in the area that patients from practices in the South Islington area may access. Appointments should be booked through your own surgery. Contact for further information: 020 7359 2010

There is some evidence to suggest that provision of self-help information may be helpful for patients with depression. Self-help information may be more useful if its use is facilitated in some way by primary care staff e.g. checking with the patient regularly how things are going and what strategies they have managed to put into place.

**Self-help information leaflets**

Copies of some recommended self-help leaflets are included in the Resource Pack accompanying these guidelines: "Depression: a self-help guide", " Anxiety: a self-help guide", "Panic: a self-help guide".

Further copies of these leaflets are available in the EMIS/Mentor Patient Information Leaflet directory or in .pdf format on the Northumberland Health Action Zone website www.northumberland-haz.org.uk/selfhelp

There is evidence for the usefulness of **exercise** in managing depression. Encourage an increase in physical activity and consider a referral for exercise on prescription where appropriate.

Encourage a **healthy and balanced diet**. There is emerging evidence about the impact of diet on mood, particularly on the negative effects of high sugar diets and thiamine deficiencies on depression. Patients should also be advised to moderate caffeine intake and reduce excessive drug or alcohol consumption.

**Sleep hygiene.** Encourage the patient to avoid sleeping during the daytime, to go to bed at a regular time each night, and to establish a healthy bedtime routine. This might include: ensuring that the evening meal is taken at least two hours before bedtime; avoiding caffeine, drugs or alcohol before bedtime; trying relaxation/ breathing exercise whilst lying comfortably in bed; not focusing on the amount of sleep that is had; and, avoiding watching TV or reading in bed, unless they have found these helpful in the past.

**Monitor and review the patient regularly**

Encourage **relapse prevention** as the patient starts to get better, i.e.:

- Encourage awareness of depressive symptoms and their triggers
- Encourage the patient to reflect on what they have learned from their experience of depression and recovering from it and to consider how these experiences can be used if they begin to feel depressed again.

**Where depression is mild these primary care management strategies are often sufficient to aid resolution of symptoms.**

- Where mild depression is more chronic and the above primary care and self-help management strategies have failed consider referral for talking therapies (see 'Psychological Management' below). If mild depression has been going on for at least two years (dysthymia) consider drug management.

- Where depression is more moderate to severe, patients are likely to benefit from drug and/or psychological management in addition to the above advice and primary care management.

**Pharmacological management**

**Choice of medication**

There is currently no evidence to suggest that medication is effective in mild depression, unless it is chronic. However antidepressant treatment should be considered and offered to patients with moderate to severe depression.

- Antidepressants are all equally efficacious (50-60% improvement compared to 30-40% on placebo) & have similar drop-out rates.
- Therefore drug choice should be tailored to the individual patient, based on patient choice, known side effect profiles, suicide risk, previous response to antidepressants, comorbidity & cost
- If the patient has responded to a particular drug in the past, use it again.
- If the patient is older or physically ill, use medication with fewer anticholinergic and cardiovascular side-effects (SSRIs are generally indicated for older people).
- If the patient is suicidal avoid tricyclics (except lofepramine) and consider dispensing a few days supply at time.
- If the patient is anxious or unable to sleep, consider a drug with more sedative effects, but warn of drowsiness and problems with driving.
- If the patient is unwilling to give up alcohol, choose one of the SSRIs that do not interact with alcohol (fluoxetine, paroxetine, citalopram).

**Good prescribing guidelines**

Once the appropriate antidepressant has been chosen, good prescribing guidelines are as follows:

**Aim for the recommended minimum effective dose**

When using tricyclics start with a low dose and titrate slowly up to the stated minimum effective dose

- If the patient has symptoms of anxiety it is also important to start SSRIs at a low dose and titrate slowly up to the recommended dose to stop "activation" of anxiety symptoms.
- Agree a follow-up plan with the patient. It is important to review patients every 1-2 weeks at start of treatment to monitor compliance and side-effects. Monitoring of suicide risk is also essential.
- Remember that non-compliance is high with antidepressants (up to 40%). It is therefore important to ask the patient to come back for review in 1-2 weeks

whether or not they have been taking their medication, so that any concerns may be addressed, or alternative management plans discussed.

- If the patient shows a poor response to antidepressants after 4-6 weeks, check compliance and consider switching to another class of drugs (See treatment guideline XX for details)
- Consider referral to the CMHT for psychiatric advice if the patient has severe depression and has not responded to two different classes of antidepressants, or if there are other concerns about risk or management.

Patients seem to have better outcomes if given **GOOD, CLEAR INFORMATION** about antidepressants – it is important to both explain the drugs you are prescribing plus give a Patient Information Leaflet.

**Drug counselling**

**Advise the patient:**

- That it will take 2-4wks to start noticing the positive effects (4-8wks in older people)
- Of the common side effects they are likely to experience – and the fact that these will usually fade in 7-10 days
- That they need to keep taking the medication regularly, even when they feel better
- That antidepressants are NOT addictive – but must not stop suddenly
- Of any necessary dosage increases, where appropriate
- To come back and see you in 1-2wks whether or not they have been taking medication
- To come back to see you immediately if they have any extreme adverse reactions to the medication e.g. sudden suicidal intent
- That they should consult you before stopping taking the medication – all antidepressants should be withdrawn slowly

Give a Patient Information Leaflet on Antidepressants – a copy of the United Kingdom Psychiatric Pharmacy Group's leaflets on SSRIs and Tricyclics are included in the Resource Pack accompanying these guidelines. Further copies in .pdf format are available at www.candi.nhs.uk/Services/pharmacy.htm

**Stopping antidepressant treatment:**

- Patients should be maintained on the same therapeutic dose for 4-6 months after their symptoms have resolved (this should be up to one year in older people).
- For patients with three or more episodes in the last 5yrs, or a total of five or more episodes, maintenance drug treatment for 5 years or indefinitely should be considered.

- Antidepressants of all classes should be withdrawn slowly over a minimum of a four-week period. This is especially true of paroxetine and venlafaxine, which have a short-half life and have been associated with a higher incidence of "discontinuation syndrome". Withdrawal can be achieved reducing dose and/or frequency (this may require switching to syrup with SSRIs). For patients who have been on longer-term maintenance pharmacotherapy the dose should be reduced over a six-month period. Fluoxetine can usually be stopped abruptly if necessary.

**Good Practice Point 3**

Give good clear information to patients when prescribing antidepressant medication - following drug counselling guidelines.

Provide an information leaflet when possible (see details above)..

**Good Practice Point 4**

When initiating a patient on antidepressants ask them to see you for a review appointment in 1-2 weeks time *whether or not they have been taking the medication*

**St Johns Wort & Depression Management**

St Johns Wort *(Hypericum perforatum)* is a popular OTC herbal remedy for treating mild depression often bought by patients.

**Evidence for effectiveness**

A Cochrane Review of 27 randomised trials concluded that:

- Hypericum is superior to placebo in the treatment of mild to moderate depressive disorders
- Hypericum has fewer short-term side-effects than older antidepressants

However,

- There is insufficient evidence to determine whether Hypericum is similarly effective or less effective than standard antidepressants
- All available trials included in the review were very short in duration (<6weeks)
- It is unclear what the standard treatment dose should be

Recommendations for clinical practice. The reviewers conclude that:

- It is difficult to base solid recommendations on currently available evidence
- The use of Hypericum might be valuable in less severe forms of depressive disorders as an alternative to "watchful waiting" or the commonly used approach of low doses (of doubtful efficacy) of tricyclics.
- There is insufficient data to recommend Hypericum for more severe forms of depression
- The preparations commercially available may vary considerable in their pharmaceutical quality and dosage of active ingredient

Linde, K., Mulrow, C.D. St Johns Wort for depression (Cochrane Review) In: *The Cochrane Library,* Issue 1, 2002.Oxford: Update Software

**Precautions**

- Preparations can induce drug-metabolising enzymes and a number of important interactions with conventional drugs have been identified. See Table below.
- The amount of active ingredient can vary between different preparations
- St Johns Wort should NOT be used in conjunction with other antidepressants because of the potential for interaction

**Known Interactions for St Johns Wort - concomitant use should be avoided**

| Drug class | Effects |
|---|---|
| Anticoagulants | Reduced anticoagulant effect of warfarin |
| Antidepressants | SSRIs – increased sertonergic effects |
| Antiepileptics | Reduced plasma conc. of carbamazepine, phenobarbital & phenytoin |

| | |
|---|---|
| Antivirals | Reduced plasma conc. of protease inhibitors, efevirenz, & nevirapine |
| Cardiac Glycosides | Reduced plasma conc. of digoxin |
| Ciclosporin | Reduced plasma conc. |
| 5HT Agonists | Increased sertonergic effects |
| Oral contraceptives | Reduced contraceptive effects |
| Theophylline | Reduced plasma conc. |

**Psychological management**
Referral for "talking therapy" is an option for all patients presenting with depression. However, the following should be considered before discussing this option with patients:

- In patients with milder depression, referral should only be considered if there has been no response to primary care management strategies. Short-term counselling may be useful in supporting adjustment to life events.
- In patients with moderate depression consider referral for talking therapies.
- In patients with severe depression, there is emerging evidence that psychological therapies (especially CBT) may be beneficial. However, it is probably important that this is used as an adjunct to pharmacotherapy, and some patients may not be able to engage in talking therapies until their more severe biological symptoms have begun to improve.

A sheet detailing the various statutory agencies for talking therapies that your practice can use is included with this pack. Details of the wide range of both statutory, voluntary and private sector talking therapy resources available in Camden & Islington are available on the Camden & Islington Mental Health Information Website at www.cimh.info/ (search under "Services – talking therapies") or in the "Counselling & Psychological Therapies Guidelines & Directory" produced by Camden & Islington MAAG (2001). The table below outlines the factors to consider in choosing the most appropriate sector.

| **NHS/Statutory sector** | **Voluntary/Grant funded** | **Private** |
|---|---|---|
| Provides statutory involvement<br>Greater liaison with | Separate from mainstream services<br>Less statutory | Greater flexibility re: appointment times<br>Longer-term therapy |

| | | |
|---|---|---|
| GPs<br>Access to other NHS mental health services<br>No fees<br>Possibly longer waiting list<br>Usually time limited treatment | involvement<br>Possibly shorter waiting list<br>Often no or low fees<br>More specialised services<br>May be time-limited | available<br>Less statutory involvement<br>May have shorter wait times<br>Fees to pay (may have sliding scale)<br>Greater control/responsibility of individual in establishing contact |

**Referral on to specialist mental health services**
Referral on to specialist secondary care mental health services should be considered if:

- The patient is at high risk of suicide or self-harm, or might need admitting to hospital. Refer, by telephone, to the **Crisis Response Team** for assessment and management.

- The patient is at moderate risk of suicide (i.e. suicidal ideation and some level of intent but no active or imminent plans) and you feel that they need more thorough or intensive assessment or monitoring than can be offered in primary care. Consider URGENT referral to the CMHT or Mental Health Services for Care of Older People (i.e. to be seen within 7 days).

- The patient has severe or atypical depression and has not responded to adequate trials of two classes of antidepressants, or you are unsure about diagnosis. Consider discussion with/routine referral to your local Community Mental Health team (CMHT) for assessment.

- The patient has other problems that need management by specialist services e.g. drug or alcohol problems.

- The patient needs a talking therapy not available in your practice. e.g.
    - Referral to the Psychology Department for Psychological Assessment and Treatment if a direct service is not provided to your surgery
    - Referral to the Psychotherapy Department (at the Whittington, Royal Free Hospital, UCH or the Tavistock for longer-term psychodynamic psychotherapy).

Guidelines about what information to include in a referral, the level of service you can expect from secondary care mental health services is detailed in the "Interface Agreement". (A copy of this is included in the Resource Pack accompanying these guidelines.)

**Remember, if you have any doubts or queries about depression management or whether to refer, discuss them with mental health professionals attached to your practice, or call your local CMHT for advice.**

**Good Practice Point 5**

> When a referral to specialist mental health services is made it should be recorded in the patients notes and/or on your practices electronic patient record using the appropriate Read Code. This will aid both individual patient management and allow practice audit and monitoring of mental health problems.

Special Considerations

***Older People***

Depressive symptoms in older people are similar to those experienced by younger people and can be just as wide ranging from occasional episodes of misery to feelings (and plans) of suicide.

**Assessment**

Certain depressive features, however, are more apparent in depressed older people, for example:

- An alteration in sleep pattern with early morning waking
- An inability to get to sleep
- Increased levels of anxiety
- An increase in physical complaints such as fatigue and gastrointestinal problems.

Although estimates of the prevalence of depression among older people vary considerably there is increasing awareness of the extent of the problem. Community studies have estimated the prevalence of depression among older people to be around 15%, with estimates double this among those attending their GP. Depression may be more common in older people because of the greater incidence of risk factors – losses, physical health problems, reduced mobility, isolation and financial/housing worries.

Depression can easily be overlooked in older people as it may be masked by co-existing physical health problems, or be seen as an inevitable consequence of ageing, rather than as a treatable disorder. Only a small number of older people with depressive disorders are specifically treated or referred to specialist secondary care providers (i.e., Psychiatrists or Community Psychiatric Nurses), and elderly people are less likely to be referred than younger people.

Treatment of depression for older people is largely the same as for younger adults. However, the following should be taken into consideration:

- People age 65 and over should be referred to the appropriate Older Adults Service, with the exception of the Crisis Response Teams who will see all emergency referrals for adults 18+ (See enclosed sheet for details of local services that your practice can refer to).

- SSRIs should be the first-line pharmacological treatment for older adults because of the anticholinergic and cardiac side effects of tricyclics. However, a significant SSRI side effect in older people is hyponatraemia.

- Older people may take longer to show an initial response to antidepressants (4-6weeks) and should be continued on a maintenance dose of an effective antidepressant for at least 12 months. However, older people often respond to a lower dose of antidepressants (refer to BNF for individual drug details).

- Psychological therapies are relevant and effective for older people too. See the MAAG directory "Older People with Psychological Health Problems: Guideline & Directory" and the Camden & Islington Mental Health Information Website www.cimh.org/ for details of local services (search under Services - Talking Therapies and Specific Issues - Older People).

***Postnatal depression***

- 10-15% of pregnancies are followed by postnatal depression (PND).
- PND does not differ significantly in presentation from depression that occurs at any other time, but it is particularly important because in addition to distress caused to the mother, it can have an adverse effect on the mother-child relationship and can compromise the child's cognitive, social and emotional development.
- PND is also a significant factor in maternal mortality through suicide.
- If PND is recognised early, and managed effectively, the outcome is good for both the mother and child.

**Assessment and diagnosis of PND**

PND is any non-psychotic depressive illness of mild-moderate severity occurring during in the first year following the baby's birth. However, it can also develop in the antenatal period. It should be distinguished from "baby blues" – the brief period of misery and tearfulness that affects around 50% of all women shortly after delivery – and puerperal psychosis, which affects between 1 in 500 and 1 in 1000 women.

The major risk factors for PND are a previous history of psychological problems; psychological problems during pregnancy; a low level of social support; a poor

marital relationship; recent adverse life experiences and "baby blues". Obstetric complications, a history of abuse and unplanned pregnancy may also be factors in addition to the risk factors for general depression.

Women should be routinely assessed during the antenatal period for a history of depression or puerperal psychosis. Pregnancy and the post-natal period are usually a time of increased contact with primary care services and therefore provide opportunities of identifying and managing mental health problems

All primary care practitioners (GPs, Practice Nurses etc.) should make opportunistic use of contacts with new mothers to ask about their emotional well-being (e.g. 6 week check, child immunisations).

In Camden & Islington, women should be screened for post-natal depression between 7-13 weeks post-delivery. This screening should be carried out routinely by trained and supervised Health Visitors, or other Community Nurses, using the Edinburgh Post-natal Depression Scale (EPDS) as a screening tool. However, it is important to recognise that the EPDS is not a diagnostic tool; that it can only be used with English speakers; and that not all Health Visitors are currently using it routinely.

Where it is used, any mothers found to have a score of 12 or over, are assessed further, and dependent on this assessment, may be offered up to four "listening visits" by the HV. The GP should also be informed, and it may be recommended that the mother sees their GP for further assessment and appropriate management.

Risk, both to the mother and the child, should be routinely assessed by health professionals in contact with the woman.

***Management of postnatal depression***

PND should be managed in the same way as non-postnatal depression, but with additional considerations, particularly regarding prescribing in pregnancy and breast-feeding.

**Primary care management**

As for non-postnatal depression.

It may be helpful to pay particular attention to the social support that the woman has available, and encourage contact with local initiatives and services where appropriate. There are often post-natal support groups available locally, and Sure Start is a useful initiative in many parts of the two boroughs. Your practice Health Visitor should be able to advise available resources.

**Pharmacological treatment**
Understandably both clinicians and women are concerned about prescribing drugs during pregnancy and lactation, and most psychotropic drugs are not licensed for use at this time. They should therefore only be prescribed with caution, and in line with the following principles:

- Establish a clear indication for treatment i.e. the presence of significant illness in the absence of acceptable or effective alternatives Use treatments in the lowest possible dose for the shortest period possible
- Drugs with a better evidence base (generally the older, more established drugs) are preferable
- Assess the benefit /risk ratio of the illness and treatment for both the mother and baby/foetus. (SIGN, 2002)

If you are unsure about prescribing in pregnancy always ask for specialist psychiatric advice or contact the **National Centre for Drugs in Pregnancy 0191 232 1525** for advice in complex cases.

**Drug treatment in the 1st trimester**

For woman who become pregnant whilst taking tricyclics or SSRI antidepressants, there is no indication to stop this therapy routinely in early pregnancy

For women who become depressed in 1st trimester, specialist advice should be sought and use antidepressant medication with caution.

**Drug treatment beyond the 1st trimester**

If antidepressants are considered clinically necessary during pregnancy, they should be maintained at the minimum effective dose, and neonates should be monitored for withdrawal symptoms

**Drug treatment and lactation**

Mothers taking tricyclics, paroxetine, sertraline or fluoxetine may continue breastfeeding provided the infant remains healthy and progress is monitored regularly

Breast-feeding should be avoided 1-2hours after medication. Where possible, use a single-dose preparation and administer this at the start of the baby's longest sleep period.

**Psychological management**
Many Health Visitors in Camden & Islington are trained in providing "listening visits" to women with high scores on the EDS. Evidence suggests that such visits may be an effective psychosocial intervention for PND. However, limits on the local availability of trained HVs mean that referral for other talking therapies should also be considered in discussion with the woman and her Health Visitor. In Sure Start areas, clinical psychology and/or counselling services may be available that offer a specific service targeted at perinatal mental health. In areas of the boroughs where

this is not available, referral to the Practice Counsellor or the Psychology Department should be considered.

**Referral to specialist services**

As with all depression, women with postnatal depression should be referred onto specialist mental health services where there is concern about risk, where there has been no response to primary care treatment, or where there is uncertainty or complexity that cannot be managed in primary care. If in doubt please contact your local CMHT to discuss further.

## Appendix O Collaborative Care Protocol

(Note in this protocol collaborative care is referred to by the term enhanced care which was the term agreed for local use with the practices.)

The study protocols are initially decided according to whether the patient is entering the study via a referral from their GP, or whether they have responded to a flyer sent to them in the post, i.e. a self-referral.

**GP Referrals**

i. The GP is asked to mention the study to an appropriate patient during their consultation, including asking if the Research Assistant (RA) can contact them; they are also asked to give out an information pack.

ii. The RA will then call the patient to ask if they have read the information sheet. The RA will offer an appointment to meet up at the surgery to discuss the study further and complete baseline measures: structured research interview, BDI, SF-12, WSAS. If the patient is happy to take part in study, they can be randomised at this point.

iii. If the patient is randomised to Treatment As Usual (TAU), the RA will inform the patient of this and advise them to contact the GP if in need of further support and explain that they have a number of options available to them, e.g. counsellor, psychologist, external organisations, etc. At this point the patient is also reminded that they will be followed up by the RA at 4 and 8 months from that day.

iv. If the patient is randomised to Enhanced Care (EC), the RA will inform the patient that the PCMHW will phone to arrange an appointment for Session 1 of their EC appointments.

**Self-Referrals**

i. The patient phones the number on the flyer/letter in order to contact the PCMHW.

ii. The PCMHW will give a brief explanation of the study over the phone. At this point it is made clear that this is a research study and not counselling or therapy. If the patient is still interested in learning more about the study and taking part, an appointment is made to meet up with the PCMHW at the surgery.

iii. An initial meeting for self-referrals lasts for approximately 45 minutes with the PCMHW, followed by approximately 15 minutes with the RA. The PCMHW explains the study including the randomisation procedure. It is made clear to the patient that there is a 50% chance of them receiving the intervention and a 50% chance of them remaining under the usual care of their GP. It is also explained that this is done in a random way by a computer programme and that it is not a choice made by any individual. The patient is made aware that the PCMHW works as part of the practice team and that while the consultation is confidential, if they were to say anything that gave cause for concern, the PCHMW would have to discuss things with the GP. The PCMHW will also inform the patient that if they were to take part in the study, they would have to make an appointment to see their GP before they

could be randomised. This is so that the patient and GP can come up with a care plan that can be supported by the PCMHW. It also allows the GP to assess the patient's eligibility to take part in the study. The patient is now asked if they would like to take part in the study. The patient is informed that as this is a research study, if they do decide to take part, a RA will be coming to ask them some research questions, but that this should not take longer than 15 minutes. If the patient does not want to take part, they are encouraged to see their GP if they would like more support.

iv. If they do want to take part in the study, the patient is asked to read through the patient information leaflet. This explains the study again including the randomisation procedure. If the patient is still happy to take part after reading this, they are asked to sign two copies of the consent form, one for the PCMHW to keep and one for the patient to keep.

v. The patient is then asked to complete the Beck Depression Inventory (BDI).

vi. Once all of this has been completed, the PCMHW administers the clinical assessment. It asks the following questions:

- What are the main problems and current symptoms?
- How long have you had your current problems?
- Have you been depressed before?
- What help have you had in the past and was there anything you found helpful? E.g. antidepressants, therapy
- Is there any additional information you would like to talk about?
- Have you discussed this with your GP?
- Are you receiving any treatment at the moment?
- Are you taking any antidepressants at the moment?
- Have you received any treatment in the last 4 months?

At the end of the session with the PCMHW, the PCMHW goes to get and introduce the RA. The RA administers a structured research interview, the BDI, SF-12 and WSAS as well as going over the study and randomisation once more. The RA will also ensure that any further questions the patient has are answered. The RA will then accompany the patient to reception for them to make an appointment to see their GP so that the GP can assess the patient's eligibility to take part in the study.

Once the GP confirms the patient's suitability, the patient can be randomised and informed of the outcome. If the patient is randomised to receive Treatment As Usual, they will receive a phone call from the RA to inform them of this. They are advised as described in the GP referral protocol above. If the patient is randomised to receive Enhanced Care, they will receive a phone call from the PCMHW to inform them of this and to arrange their first Enhanced Care session.

Once the patient has been randomised to receive Enhanced Care, they will each receive around three sessions with the PCMHW and several phone calls if required by the patient. This is the same regardless of whether the patient has entered the study as a GP referral or a self-referral. As a result of the initial meeting with the

PCMHW received by all self-referrals, the first session will be slightly different according to the entry route of the patient.

**GP referral session 1**
When a GP referral is randomised to Enhanced Care, they have only met or spoken to the RA and have not met the PCMHW.

In the first session, the PCMHW will introduce themselves and begin by setting out the length of time allowed for the session and briefly explaining the structure of the session. The PCMHW will also answer any questions that the patient may have. It is important for the PCMHW to emphasize that they are not a therapist or counsellor and that they will not be receiving counselling or therapy. The PCMHW will also make clear the confidentiality of the study as is discussed in the self-referral initial meetings.

At this point, the PCMHW will explain the format of the intervention, i.e. that they will meet two or three times over the upcoming 4 months and that this can be on the telephone if they would prefer. The patient is also reminded that they will be followed up at 4 and 8 months by the RA they met previously.

If the patient is clear about everything, the session will proceed with the clinical assessment as described above in the initial meeting for self-referrals (without asking whether they have discussed things with their GP).

The next part of the session will proceed according to whether or not the patient has been prescribed antidepressants:

1. ANTIDEPRESSANTS
Patients who have been prescribed antidepressants are asked about these following a structured interview. The following questions are asked:

- Have you been prescribed any antidepressants?
- Have you experienced any side effects? If yes, the PCMHW will record any recommendations given, e.g. sucking boiled sweets if the side effect is a dry mouth, suggestions to return to the GP.
- Their thoughts about taking medication.
- Any concerns about their medication.
- How they are taking their medication, e.g. whether they forget to take a dose, whether they take it regularly or sometimes stop taking it, whether they take different doses to those instructed.

At this point, the session may come to a natural end time-wise. If this is the case, the PCMHW will thank the patient for attending the session, describe what will happen next and ask the patient if they would like to make another appointment in 2-3 weeks time. The PCMHW will also let the patient know that they will telephone them in 1 week to see how they are getting on with the antidepressants and answer

any questions/concerns. If the patient has few or no concerns or questions regarding their antidepressants, this part of the consultation may be very brief.

If this is the case, the PCMHW may introduce the idea of facilitated self-help at this point in the consultation, and this would follow the protocol for "No antidepressants" as set out below.

2. NO ANTIDEPRESSANTS

If the patient has not been prescribed antidepressants, there will be more time left in the session to introduce facilitated self-help. The PCMHW explains that facilitated self-help offers an alternative way for people to work on their problems at their own pace. It is not intended to resolve all your problems at once, but gives an idea of things you can do to cope with them in a better way. There are three booklets which are offered to the patient that they might be interested in looking at. The patient can be advised that a lot of people who have been feeling a similar way to themselves have found them to be really useful.

The PCMHW explains that the booklets are based on the model of cognitive behavioural therapy and if the patient is unfamiliar with the model it is explained in a simple clear way using examples. A one line explanation such as "we know that what a person thinks, affects the way they feel and what they do and the idea of the model is that changing one aspect of the model will have an effect on the other aspects of it" is often enough.

It is often helpful for the PCMHW to offer a neutral example to demonstrate the model, e.g.:
"Imagine that you are alone in the house at night and you hear a noise coming from somewhere upstairs. If your first instinct is that someone is trying to break in, you would be very scared and start panicking. Your palms would start sweating and your heart would start racing. This would cause you to go upstairs and check the rooms of the house and make sure no-one's there. On the other hand, if you heard the same noise and automatically thought that it was just the boiler making noises, you would not have the same physical feelings of fear and panic. You would also not produce the behaviours of checking the rooms in the house".

The PCMHW will explain that by using the booklets, they can identify techniques that will help them to deal with their current difficulties. If it is helpful for the patient, they can discuss the exercises and even do some together with the PCMHW if they think they would find it helpful. The PCMHW will also reiterate that they are not a therapist. The patient is also encouraged to practice the exercises at home in between sessions with the PCMHW, whose role will then be to support their interest in learning new ways of managing their depression.

At the end of the session the PCMHW will ask if the patient has any questions about anything discussed during the session, or if there is anything else they would like to talk about. The PCMHW will then offer another appointment in 2-3 weeks time to see how the patient has got on with the booklets (the patient will be asked to bring the booklets with them to the next appointment).

If the patient is not interested in facilitated self-help or does not want to take the booklets, this is also supported. The patient is offered an appointment in 2-3 weeks or a phone call if they would prefer.

**Self-Referral Session 1**
Self-referrals will have met the PCMHW during the initial meeting and will therefore have done the clinical assessment. The patient is reminded about enhanced care and how it will work, e.g. length of session, number of sessions within a 4-month treatment period. The PCMHW will enquire into how things have been since they last met and how their consultation with the GP went.

The consultation will then proceed in the same way as a GP referral would during session 1. If the patient has been prescribed antidepressants, they will be supported as described above. If not, they will be offered facilitated self-help as described above.

From session 2 onwards, the meetings are the same, regardless of whether the patient was a GP- or self-referral.

**Session 2**
The PCMHW will begin by setting out the structure of the session including how long they have for the session (30 minutes). Following this, the PCMHW will ask how things have been since the last meeting, i.e. any problems, GP consultations etc.

If the patient is taking antidepressants, they are asked the same questions as described above in session 1. Once the PCMHW and patient are happy about antidepressant use, facilitated self-help can be introduced as described above if it had not been already.

If this is the second session of self-help, the session will focus on discussing the following questions:

- What are the patient's aims?
- What would life be like it the patient was feeling better?
- What would you need to change to get there?
- Has the patient read the booklets?
- Which parts of them was the patient directed to?
- Is the patient using any of the exercises?
- Have the booklets been helpful?
- Have their been any difficulties?

It is not always appropriate or relevant to ask each of the questions. A general discussion about the self-help and how the patient has got on with it often answers them anyway. If it is helpful, the PCMHW and patient might go through some of the exercises together.

If the patient has not looked at the exercises and/or does not want to use the self-help approach, the PCMHW will talk about options that are available for the patient and what they would like to do for things to move forward. It is sometimes possible for the PCMHW to discuss and recommend some of the self-help approaches without using the booklets.

**Session 3**

The third session will be the final one if facilitated self-help has been introduced in session 1. Patients on antidepressants who were not introduced to the self-help until their second session will see the PCMHW one extra time as this will be their second session of self-help.

The format of the session is the same as the first two, with the length of session and structure stated at the beginning. This will usually be a shorter meeting of maybe only 20 minutes. Antidepressant questions will be asked if necessary. The patient will also be asked how things have been since they last saw the PCMHW. This may be particularly relevant if the final session is some weeks since the second one.

The PCMHW will then follow up the self-help using the same questions as above in session 2. The PCMHW will then ask the patient whether they think they could notice any signs that their improvement was slipping. The patient will be directed toward the section in the booklets on relapse and setbacks. This will also be discussed during the session and the patient will be reminded that having a bad day or a lapse does not mean that they are becoming depressed again. Reassurance will be given that it is normal to have bad days and that ups and downs are a part of everyday life for everyone.

If the patient has not been interested in the self-help, the PCMHW will ask how things have been since they last met. If the patient has been feeling better, the PCMHW will discuss whether there has been anything in particular that has helped them to feel this way or why they think things have been a bit better for them. If things have not been good, the PCMHW will again ask why they think this might be and what they think they might need to do to feel better. The PCMHW will also discuss relapse and setbacks with the patient in the same way as above.

If at any point the patient indicates that they would like to see someone else, e.g. a counsellor or psychologist, the PCMHW will encourage the patient to make an appointment to discuss things with their GP and the PCMHW will also mention how the patient feels to the GP.

At the end of the session, the PCMHW will remind the patient that the 4-month treatment period has come to an end and that they will be followed up by the RA. The patient will be thanked for their participation in the study and encouraged to go back to their GP at any point in the future if they need any more support.

**Session 4**

If the patient was introduced to facilitated self-help in their second session, session 4 would be their final meeting with the PCMHW and would proceed as described above in session 3.

**Phone calls**
If the patient is prescribed antidepressants, either at the start of the intervention or at any time during it, they are given a phone call one week afterwards. The PCMHW will ask the same questions as those described earlier for antidepressant support.

For some patients, a phone call is more appropriate than meeting at the surgery for session 2, 3 or 4. In this case, the phone call would take the same format as a meeting face to face with the same questions being asked. The patient would be given the same opportunity for support and to ask any questions they might have.

Many patients are offered additional phone calls in between meeting with the PCMHW worker at the surgery. These calls are likely to take a similar format to those taking the place of face to face meetings. The patient is asked how things have been and if there is anything that they would like to talk about. If they are taking antidepressants their use of these is supported, as it would be if they are using facilitated self-help.

**Enhanced care patients who are referred to the counsellor, psychologist or elsewhere**
Not all patients referred to Enhanced Care will need to see the PCMHW regularly over the 4-month intervention period. This is especially the case if they are referred on elsewhere.

In these cases, the initial meeting and session 1 for self-referrals or session 1 for GP referrals will be the same as described earlier. Once the patient has seen the PCMHW for session 1, the PCMHW will offer the patient a phone call once a month to see how things are going and support their work with the counsellor/psychologist, etc.

If the patient is put onto a waiting list to see someone, they may wish to see the PCMHW in the normal way over the 4-month period.

## Appendix P Trial Information

(Note: in these information sheets collaborative care is referred to by the term enhanced care which was the term agreed for local use with the practices.)

### 1. PATIENT INFORMATION SHEET – GP referral direct to study
### Enhanced Care Treatment for Depression Study

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

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**What is the purpose of the study?**
Depression is one of the most common problems in GP practices. It is estimated that one in four people will suffer from depression at some point in their lifetime. Depression can be treated in a variety of ways, but more studies are needed to develop the most effective ways to help people get access to and make best use of use these treatments.
Some research studies have shown that if GP practices enhance the care they can provide for people with depression, by involving additional staff who can provide those people with extra support, they can help people recover more quickly. We are aiming to develop this work further by placing primary care mental health workers (PCMHWs) in a number of GP practices in Camden. They will be able to provide support for people prescribed antidepressant medication, provide information and 'self-help' materials about dealing with depression, support people who are referred on to other services and provide informal support. They can also work with the practice to help them identify people who might be suffering from depression and who could be offered help. This new research will evaluate how effective this additional support is for people with depression and see whether it adds anything to usual care.

**Why have I been chosen?**
You have recently been seen by your GP who has identified you as having depression and you have expressed an interest in being involved in the study.

**Do I have to take part?**

*It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.*

**What will happen to me if I take part?**

If you decide to take part in the study, the researcher will ask you to complete some short questionnaires that ask you about your current problems. You will then be randomised to receive one of two different interventions.

Sometimes, because we do not know which way of treating patients is best, we need to make comparisons. People will be put into different intervention groups and then compared. The groups are selected by a computer which has no information about the individual – i.e. selection is by chance. Patients in each group then have a different intervention and these are compared. We have two groups in this study and therefore, you will have 50% chance of getting each one of the intervention groups.

**Intervention groups**

**1) Usual GP Care**

This is routine care as provided by your GP. If you receive this treatment you will see your GP as required and will receive the full range of treatments normally available.

**2) Enhanced Care**

If you receive this treatment, then as well as seeing your GP as needed, you would be offered an initial meeting with the primary care mental health worker (PCMHW). At this meeting, the PCMHW will provide you with some information about depression. You and your GP will decide on a treatment plan and whichever treatment option you chose, you will be followed up by the PCMHW over the next 4 months by a mixture of phone contact and face-to-face meetings (most likely between two or six contacts). During these meetings you will have the opportunity to discuss with the PCMHW any difficulties you may have during the course of your treatment.

Below are some examples showing how the PCMHW might work with you depending on which treatment you receive:

a) **Anti-depressant Medication**: If you chose this treatment you will be prescribed anti-depressant medication by your GP and be offered follow-up contacts from the PCMHW over the next 4 months, both on the phone and by visits to the surgery. They will discuss with you how you are feeling and getting on with the medication, any concerns about using it, and give you information about common side effects. They will work closely with your GP, who you will also see you for follow-ups as usual.

b) **Self-help:** If you chose this option the PCMHW will provide you with the self-help materials and some instructions about its use. These materials contain information about the nature of your symptoms and will help you to learn new ways of coping with them based on psychological methods. During the follow-up contacts, the PCMHW will ask you what self-help strategies you are using and answer your questions about the materials. The PCMHW will also support you to

formulate a plan for the use of these methods in the future in order to maintain the gains achieved and protect you from sliding back into depression.

c) **Referral to other services**: If you are referred on to another service (this may be counselling or something else) the PCMHW will offer you follow-up contact over the next 4 months to make sure that you linked up alright with the service and check how things are going.

The researcher will contact everyone taking part in the study after 4 and 8 months to ask you to complete some further questionnaires to see if your problems have changed. We are interested in learning about your experience and satisfaction with treatment and the researcher will ask you a number of questions about this in addition to asking you to fill in the questionnaires. To help record people's responses accurately and to help with analysis of the information, we will record interviews on audiotape and then transcribe them. Once the research has been completed these tapes will be destroyed. They will not at any stage be available to anyone outside the research group.

**What do I have to do?**

During the study period, apart from attending appointments as required, you can carry on life as normal.

**What are the possible benefits of taking part?**

The information we get from this study may help us to improve the care of people with depression in primary care in the future.

**What happens when the research study stops?**

The information collected will be written up in a report. It will be presented to staff planning local services and will be used to influence local service developments. We will also publish our results in a journal read by people planning and researching mental health services and will hope also to make them available in a form accessible to service users. A summary of the results will be made available to all participants.

**What if I am unhappy with the research?**

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of the research, the research team will of course be very happy to discuss this with you. They are also happy to explain the study further if you have questions not answered by this sheet. Their contact details are at the end of this form. The normal National Health Service complaints mechanisms are of course also available to you.

**Will my taking part in the research be kept confidential?**

You will be asked to give written consent for the research team to access your medical records. All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the

surgery will have your name and address removed so that you cannot be recognised from it. When we report on the research, it will not be in anyway possible to identify you from the report.

**Who is organising the research?**

This study is organised by Camden PCT and the Centre for Outcomes Research and Effectiveness (CORE) at University College London. It has been reviewed by the Camden & Islington Community Health Service Local Research Ethics Committee.

**Contact for further information**

If you require any further information or have any comments or concerns please feel free to contact **Judy Leibowitz on 0207 445 8580** (project supervisor, Camden PCT).

Thank you for considering taking part in this study. If you consent to taking part please read and sign the attached consent form. You will be given a copy of the information sheet and a signed consent form to keep.

## 2. PATIENT INFORMATION SHEET – identified from EMIS
## Enhanced Care Treatment for Depression Study

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

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**What is the purpose of the study?**
Depression is one of the most common problems in GP practices. It is estimated that one in four people will suffer from depression at some point in their lifetime. Depression can be treated in a variety of ways, but more studies are needed to develop the most effective ways to help people get access to and make best use of use these treatments.
Some research studies have shown that if GP practices enhance the care they can provide for people with depression, by involving additional staff who can provide those people with extra support, they can help people recover more quickly. We are aiming to develop this work further by placing primary care mental health workers (PCMHWs) in a number of GP practices in Camden. They will be able to provide support for people prescribed antidepressant medication, provide information and 'self-help' materials about dealing with depression, support people who are referred on to other services and provide informal support. They can also work with the practice to help them identify people who might be suffering from depression and who could be offered help. This new research will evaluate how effective this additional support is for people with depression and see whether it adds anything to usual care.

**Why have I been chosen?**
You have recently been seen by your GP who has identified you as having depression.

**Do I have to take part?**

*It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.*

**What will happen to me if I take part?**
If you decide to take part in the study, the researcher will ask you to complete some short questionnaires that ask you about your current problems. You will then be randomised to receive one of two different interventions.

Sometimes, because we do not know which way of treating patients is best, we need to make comparisons. People will be put into different intervention groups and then compared. The groups are selected by a computer which has no information about the individual – i.e. selection is by chance. Patients in each group then have a different intervention and these are compared. We have two groups in this study and therefore, you will have 50% chance of getting each one of the intervention groups.

**Intervention groups**

**1) Usual GP Care**

This is routine care as provided by your GP. If you receive this treatment you will see your GP as required and will receive the full range of treatments normally available.

**2) Enhanced Care**

If you receive this treatment, then as well as seeing your GP as needed, you would be offered an initial meeting with the primary care mental health worker (PCMHW). At this meeting, the PCMHW will provide you with some information about depression. You and your GP will decide on a treatment plan and whichever treatment option you chose, you will be followed up by the PCMHW over the next 4 months by a mixture of phone contact and face-to-face meetings (most likely between two or six contacts). During these meetings you will have the opportunity to discuss with the PCMHW any difficulties you may have during the course of your treatment.

Below are some examples showing how the PCMHW might work with you depending on which treatment you receive:

d) **Anti-depressant Medication**: If you chose this treatment you will be prescribed anti-depressant medication by your GP and be offered follow-up contacts from the PCMHW over the next 4 months, both on the phone and by visits to the surgery. They will discuss with you how you are feeling and getting on with the medication, any concerns about using it, and give you information about common side effects. They will work closely with your GP, who you will also see you for follow-ups as usual.

e) **Self-help:** If you chose this option the PCMHW will provide you with the self-help materials and some instructions about its use. These materials contain information about the nature of your symptoms and will help you to learn new ways of coping with them based on psychological methods. During the follow-up contacts, the PCMHW will ask you what self-help strategies you are using and answer your questions about the materials. The PCMHW will also support you to formulate a plan for the use of these methods in the future in order to maintain the gains achieved and protect you from sliding back into depression.

f) **Referral to other services**: If you are referred on to another service (this may be counselling or something else) the PCMHW will offer you follow-up contact over the next 4 months to make sure that you linked up alright with the service and check how things are going.

The researcher will contact everyone taking part in the study after 4 and 8 months to ask you to complete some further questionnaires to see if your problems have changed. We are interested in learning about your experience and satisfaction with treatment and the researcher will ask you a number of questions about this in addition to asking you to fill in the questionnaires. To help record people's responses accurately and to help with analysis of the information, we will record interviews on audiotape and then transcribe them. Once the research has been completed these tapes will be destroyed. They will not at any stage be available to anyone outside the research group.

**What do I have to do?**

During the study period, apart from attending appointments as required, you can carry on life as normal.

**What are the possible benefits of taking part?**

The information we get from this study may help us to improve the care of people with depression in primary care in the future.

**What happens when the research study stops?**

The information collected will be written up in a report. It will be presented to staff planning local services and will be used to influence local service developments. We will also publish our results in a journal read by people planning and researching mental health services and will hope also to make them available in a form accessible to service users. A summary of the results will be made available to all participants.

**What if I am unhappy with the research?**

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of the research, the research team will of course be very happy to discuss this with you. They are also happy to explain the study further if you have questions not answered by this sheet. Their contact details are at the end of this form. The normal National Health Service complaints mechanisms are of course also available to you.

**Will my taking part in the research be kept confidential?**

You will be asked to give written consent for the research team to access your medical records. All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the surgery will have your name and address removed so that you cannot be recognised from it. When we report on the research, it will not be in anyway possible to identify you from the report.

**Who is organising the research?**

This study is organised by Camden PCT and the Centre for Outcomes Research and Effectiveness (CORE) at University College London. It has been reviewed by the Camden & Islington Community Health Service Local Research Ethics Committee.

**Contact for further information**

If you require any further information or have any comments or concerns please feel free to contact **Judy Leibowitz on 0207 445 8580** (project supervisor, Camden PCT).

Thank you for considering taking part in this study. If you consent to taking part please read and sign the attached consent form. You will be given a copy of the information sheet and a signed consent form to keep.

## 3. PATIENT INFORMATION SHEET – Recruitment via flyer

### Enhanced Care Treatment for Depression Study

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

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**What is the purpose of the study?**

Depression is one of the most common problems in GP practices. It is estimated that one in four people will suffer from depression at some point in their lifetime. Depression can be treated in a variety of ways, but more studies are needed to develop the most effective ways to help people get access to and make best use of use these treatments.

Some research studies have shown that if GP practices enhance the care they can provide for people with depression, by involving additional staff who can provide those people with extra support, they can help people recover more quickly. We are aiming to develop this work further by placing primary care mental health workers (PCMHWs) in a number of GP practices in Camden. They will be able to provide support for people prescribed antidepressant medication, provide information and 'self-help' materials about dealing with depression, support people who are referred on to other services and provide informal support. They can also work with the practice to help them identify people who might be suffering from depression and who could be offered help. This new research will evaluate how effective this additional support is for people with depression and see whether it adds anything to usual care.

**Why have I been chosen?**

You contacted the practice after being sent a flyer through the post and have identified yourself as possibly having depression. You have expressed an interest in being involved in the study.

**Do I have to take part?**

*It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.*

**What will happen to me if I take part?**

If you decide to take part in the study, you will initially be asked some questions by the Primary Care Mental Health Worker and the researcher will ask you to complete some short questionnaires that ask you about your current problems. If they think you may be depressed an after learning more about the study you are interested in taking part then they will ask you to see your GP. If your GP considers that you are depressed. You will then be randomised to receive one of two different interventions.

Sometimes, because we do not know which way of treating patients is best, we need to make comparisons. People will be put into different intervention groups and then compared. The groups are selected by a computer which has no information about the individual – i.e. selection is by chance. Patients in each group then have a different intervention and these are compared. We have two groups in this study and therefore, you will have 50% chance of getting each one of the intervention groups.

**Intervention groups**

**1) Usual GP Care**

This is routine care as provided by your GP. If you receive this treatment you will see your GP as required and will receive the full range of treatments normally available.

**2) Enhanced Care**

If you receive this treatment, then as well as seeing your GP as needed, you would be offered an initial meeting with the primary care mental health worker (PCMHW). At this meeting, the PCMHW will provide you with some information about depression and then you will be followed up over the next 4 months by a mixture of phone contact and face-to-face meetings (most likely between two or six contacts). During these meetings you will have the opportunity to discuss with the PCMHW any difficulties you may have during the course of your treatment.

Below are some examples showing how the PCMHW might work with you depending on which treatment you receive: (you can receive more than one of the following)

g) **Anti-depressant Medication**: If you receive this treatment you will be prescribed anti-depressant medication by your GP and be offered follow-up contacts from the PCMHW over the next 4 months, both on the phone and by visits to the surgery. They will discuss with you how you are feeling and getting on with the medication, any concerns about using it, and give you information about common side effects. They will work closely with your GP, who you will also see you for follow-ups as usual.

h) **Self-help:** If you chose this option the PCMHW will provide you with the self-help materials and some instructions about its use. These

materials contain information about the nature of your symptoms and will help you to learn new ways of coping with them based on psychological methods. During the follow-up contacts, the PCMHW will ask you what self-help strategies you are using and answer your questions about the materials. The PCMHW will also support you to formulate a plan for the use of these methods in the future in order to maintain the gains achieved and protect you from sliding back into depression.

i) **Referral to other services**: If you are referred on to another service (this may be counselling or something else) the PCMHW will offer you follow-up contact over the next 4 months to make sure that you linked up alright with the service and check how things are going.

The researcher will contact everyone taking part in the study after 4 and 8 months to ask you to complete some further questionnaires to see if your problems have changed.

We are interested in learning about your experience and satisfaction with treatment and the researcher will ask you a number of questions about this in addition to asking you to fill in the questionnaires. To help record people's responses accurately and to help with analysis of the information, we will record interviews on audiotape and then transcribe them. Once the research has been completed these tapes will be destroyed. They will not at any stage be available to anyone outside the research group.

**What do I have to do?**

During the study period, apart from attending appointments as required, you can carry on life as normal.

**What are the possible benefits of taking part?**

The information we get from this study may help us to improve the care of people with depression in primary care in the future.

**What happens when the research study stops?**

The information collected will be written up in a report. It will be presented to staff planning local services and will be used to influence local service developments. We will also publish our results in a journal read by people planning and researching mental health services and will hope also to make them available in a form accessible to service users. A summary of the results will be made available to all participants.

**What if I am unhappy with the research?**

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of the research, the research team will of course be very happy to discuss this with you. They are also happy to explain the study further if you have questions not answered by this sheet. Their contact details are at the end of this form. The normal National Health Service complaints mechanisms are of course also available to you.

**Will my taking part in the research be kept confidential?**

You will be asked to give written consent for the research team to access your medical records. All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the surgery will have your name and address removed so that you cannot be recognised from it. When we report on the research, it will not be in anyway possible to identify you from the report.

**Who is organising the research?**

This study is organised by Camden PCT and the Centre for Outcomes Research and Effectiveness (CORE) at University College London. It has been reviewed by the Camden & Islington Community Health Service Local Research Ethics Committee.

**Contact for further information**

If you require any further information or have any comments or concerns please feel free to contact **Judy Leibowitz on 0207 445 8580** (project supervisor, Camden PCT).

Thank you for considering taking part in this study. If you consent to taking part please read and sign the attached consent form. You will be given a copy of the information sheet and a signed consent form to keep.

## 4. PATIENT LETTER TO ACCOMPANY FLYER – YOUNG MEN

Dear XXXX

We are writing to let you know about a new service for patients, which has started here at *XXXX* Practice, as part of a research study coordinated by University College London and Camden and Islington NHS Trust.

We are sending flyers to all men between 16 and 35 registered with *XXXX* Practice. We are targeting this age group because we know that they are often dealing with emotional problems on their own, and this can be overwhelming at times.

> Everyone feels sad or low at times- it's a normal part of life, particularly if you are going through personal difficulties (e.g. exams, work, money or relationship problems). However, when these feelings don't go away and stop us from doing the things we usually do, they could signal depression. Sometimes it's hard to take that first step and ask for help, but there is no reason to feel ashamed or embarrassed.

By contacting the above number patients will be able to speak to a specially trained **Primary Care Mental Health Worker**, *Name Inserted* , who is working at *XXXX* as part of the study, and she can offer an appointment to see her at the practice.

We are evaluating this service over the next year and it will be available to patients over 16, both male and female, who are registered with us and have not received any treatment, antidepressants or psychological therapy, in the last 4 months. If you think you, or someone you know who is registered with us, may be depressed, then this new service may help. We have enclosed a flyer with more information about depression and its symptoms.

If you are not interested in taking part in the study, or if you decide to withdraw at any time, your usual treatment at the practice will not be affected in any way.

With best wishes,

*Patient's GP*

## 5. PATIENT LETTER TO ACCOMPANY FLYER – PREVIOUS EPISODE

Dear XXXX

We are writing to let you know about a new service for patients, which has started here at *XXXX* Practice, as part of a research study coordinated by University College London and Camden PCT

We are sending flyers to a selection of patients registered with *XXXX* Practice who have previously mentioned to their GP that they have experienced emotional difficulties. Everyone feels sad or low at times- it's a normal part of life, particularly if you are going through personal difficulties (e.g. work, money or relationship problems). However, when these feelings don't go away and stop us from doing the things we usually do, they could signal depression. Sometimes it's hard to take that first step and ask for help.

By contacting the number below, patients will be able to speak to a specially trained **Primary Care Worker**, *Name Inserted*, who is working at Ampthill Square as part of the study, and she can offer an appointment to see her at the practice.

We are evaluating this service over the next year and it will be available to patients over 16, both male and female, who are registered with us and have not received any treatment, antidepressants or psychological therapy, in the last 4 months. If you think you, or someone you know who is registered with us, may be depressed, then this new service may help. The enclosed flyer has more information about depression and its symptoms.

If you are not interested in taking part in the study, or if you decide to withdraw at any time, your usual treatment at the practice will not be affected in any way.

With best wishes,

Patient's GP

## 6. PATIENT LETTER TO ACCOMPANY FLYER - Chronic physical illness

Dear Patient name,

The *XXXX* Practice is taking part in a research study on depression co-ordinated by University College London and Camden Primary Care Trust, in which they will be evaluating the role of a specially trained Primary Care Worker in supporting people with depression.

We are sending letters to patients registered with the practice who are affected by a long-term physical illness. This is because we know that mood and emotions can be affected by physical health. People with illnesses, such as heart disease or arthritis, may find it hard to cope sometimes for a variety of reasons. These can include difficulties with physical pain or getting used to a different lifestyle as a result of the illness. Treatment can also sometimes be difficult to take, for example, medication with unpleasant side effects. All this could lead to low mood, or losing the motivation to do things that were once enjoyable. Other symptoms may include a change in appetite or sleeping habits, poor concentration, fatigue or restlessness.

When these feelings persist they can interfere with normal activities. This could be a sign of depression. Depression can be a difficult problem to cope with and sometimes it is hard to ask for help.

If you identify with the type of problems described in this letter, you can contact *name inserted,* the **Primary Care Worker** on the below number. She can give you more information about taking part in the study, and can offer you an initial appointment to see her at the surgery to discuss your difficulties. Patients who take part in the study must be over 16 years old, registered with the practice and they must not have taken any medication or had any psychological therapy for depression in the past 4 months.

This study is trying to find out if receiving support from a Primary Care Worker is more helpful to patients with depression, compared to normal care from their GP. This means that some patients in the study will continue their care under their GP as normal, and some patients will have contact with the Primary Care Worker over a period of four months, in addition to GP care. Patients are put into one of these two groups in a random way (i.e. the practice team does not decide).

If you are not interested in taking part in the study, or if you decide to withdraw at any time, your usual treatment at the practice will not be affected in any way.

With best wishes,

Patient's GP

7. ***FLYER – Young men***

**8.** ***FLYER – Previous episodes***

## 10. PATIENT LETTER - identified by EMIS GP follow-up letter

Dear *Patient name,*

**RE: Evaluation of a new Service for Depression in the practice**

Following our recent consultation, I am writing to let you know about a new service that we are involved in evaluating at the practice that you may find helpful.

We are looking at the effect of offering additional support to people with depression. It will involve a primary care mental health worker, (*name*), who can be in touch with you over the next four months to help give you some support and advice about depression.

I enclose a leaflet with more information about the study as well as a leaflet on depression. You will also find a few brief questionnaires, if you are interested in being involved in the study the researcher Olga Luzon will go through with you over the phone or here at the practice. If you are interested, or would like to know more about this study, please ring and leave your contact details for *XXXX* on *NNN NNN NNN*.

Please notice that your involvement is optional and if you are not interested in this study, your usual treatment will not be affected in any way.

Should you require any further clarification, please do not hesitate to contact the practice or *XXXX* directly who will be happy to respond to your questions.

With best wishes,

Patient's GP

Enc: patient info sheet

## Appendix Q Trial Questionnaires and Assessments

### 1. Baseline Questionnaire

**PATIENT NUMBER** ☐

Name of RA: _____

Date of Interview: _____ Duration Interview: _____

*Personal Information*

Patient's Name : _____

Patient's tel. no: _____

Date of Birth/Age: _____ Male ☐ Female ☐

Patient's Address: _____

_____

_____

Practice Name: _____

Self-referral ☐

GP referral ☐ Name of GP: _____

Other Name of professional: _____

Randomisation: EC ☐ TAU ☐

Patient **not** in trial: *reason*

_____

_____

_____

_____

**1.** Ethnic Background:

01 White

02 White European

03 Caribbean

04 Black, African

05 Black, Other _____

06 Indian

07 Pakistani

08 Bangladeshi

09 Chinese

10 Irish

11 Greek/Greek Cypriot

12 Turkish/Turkish Cypriot

13 Filipino

14 Eritrean

15 Somali

16 Mixed Parentage

17 Arab

18 Other _____

**2.** First language: English ☐ Other ☐

_____

**3.** Education:

Age left school / formal education: _____

Highest level of education achieved: _____

**4.** Currently employed: Yes ☐ No ☐

If yes, then occupation: _____

**5.** In receipt of benefits: Yes ☐ No ☐

If yes, then type of benefit: _____

Occupation of head of household: _____

**6.** Type of accommodation:

☐ Homeowner

☐ Private rental

☐ Council house

☐ Other _____

**7.** Relationships/Social Support *(tick all that apply)*

☐ Living alone *(not including dependents)* ☐ Full time carer

☐ Living with partner ☐ Living in shared accommodation

☐ Caring for children under 5 years ☐ Living in temporary accommodation

☐ Caring for children over 5 years

☐ Living in institution/hospital

☐ Living with parents/guardian

☐ Living with other relatives/friends

☐ Other/s _____

8. Socioeconomic status *(Census)*

☐ I-IIIa ☐ IIIb-V

9. Have you been depressed before?

☐ No

☐ Yes ☐ once *(excluding now)* ☐ times or more

10. Family history of Depression?

☐ No ☐ Yes

11. Do you use alcohol? ☐ No ☐ Yes

*1 drink = 1/2 pint of beer or 1 glass of wine or 1 single spirits*

MEN: How often do you have EIGHT or more drinks on one occasion?

WOMEN: How often do you have SIX or more drinks on one occasion?

☐ Never ☐ Less than monthly ☐ Monthly

☐ Weekly ☐ Daily or almost daily *(NO NEED to ask the following questions)*

How often during the last year you have been unable to remember what happened the night before because you had been drinking?

☐ Never ☐ Less than monthly ☐ Monthly

☐ Weekly ☐ Daily or almost daily

How often during the last year have you failed to do what was normally expected from you because of drinking?

☐ Never ☐ Less than monthly ☐ Monthly
☐ Weekly ☐ Daily or almost daily

In the last year has a relative or friend or a doctor or other health worker been concerned about your drinking or suggested you cut down?

☐ No ☐ Yes, on one occasion ☐ Yes, on more than one occasion

**11.** Have you used drugs other than those required for medical reasons in the last year?

☐ No ☐ Yes, what, how often, length of time using?

_____
_____
_____
_____

Has this cause you any problems?

☐ No ☐ Yes

**12.** Additional Information

_____
_____
_____

**2. Follow-up Questionnaire – Usual Care**

## Guidelines for filling in follow-up questionnaire

- Please read each question carefully and answer as best you can.
- Try not to spend too long thinking about each question, going with your first reaction is often the best way.
- Please answer every question and do not leave any questions out.
- When answering the questions that require more than a ticked box, please answer as fully as you feel you can, but you do not have to use up all the space provided.
- Please write clearly, so that we can read what you have written without difficulty.
- Everything you tell us is confidential.
- **Thank you** for taking the time to complete this questionnaire. Your answers are very important to our research.

# Follow-up Questionnaire: TAU

## How you feel now

1. Overall, how would you say you feel now compared to how you felt when you first contacted us?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| I feel a lot worse | I feel slightly worse | I feel neither better nor worse | I feel somewhat better | I feel a lot better |

## *Other treatment*

2. During the last 4 months have you had any treatment for depression?

| ☐ | ☐ |
|---|---|
| Yes | No |

3. If Yes, what treatment did you receive? Tick all that apply

- ☐ Prescribed medication
- ☐ Referral for talking therapy e.g. counsellor/ psychologist
- ☐ Advice from your GP
- ☐ Psychiatric assessment
- ☐ Other: _____

4. If referred on to somewhere else, did you attend appointments?

☐ Yes ☐ No ☐ Does not apply

## Medication

5. If you have been prescribed antidepressant medication, please answer the following:

| | Yes | No |
|---|---|---|
| Do you ever forget to take your antidepressants? | ☐ | ☐ |
| Are you careless at times about taking your antidepressants? | ☐ | ☐ |
| When you feel better, do you sometimes stop taking your antidepressants? | ☐ | ☐ |
| Sometimes when you feel worse, do you stop taking your antidepressants? | ☐ | ☐ |

### Your reasons for seeking help and your comments on the services

*This section contains questions about services you have received. The services you have received means all the help you have had. This might include advice from your GP, anti-depressants, or counselling.*

6. Why did you decide to ask for help with your depression on this occasion?

_____

7. What problems were you hoping would be helped by the services you received?

8. Which parts of the services did you find most helpful, and can you say why?

9. Have the services you received helped you have a better understanding of why you became depressed?

10. Do you think the services could be changed in any way, to make them more helpful?

11. If you did not complete any of the services you were offered (including anti-depressants, counselling etc.), could you give your reasons?

12. Do you have any other comments about the services?

### 3. Follow-up Questionnaire – Collaborative Care

**Guidelines for filling in follow-up questionnaire**

- Please read each question carefully and answer as best you can.
- Try not to spend too long thinking about each question, going with your first reaction is often the best way.
- Please answer every question and do not leave any questions out.
- When answering the questions that require more than a ticked box, please answer as fully as you feel you can, but you do not have to use up all the space provided.
- Please write clearly, so that we can read what you have written without difficulty.
- Everything you tell us is confidential.
- **Thank you** for taking the time to complete this questionnaire. Your answers are very important to our research.

## Follow-up Questionnaire: EC
## Enhanced Care for Depression Study

How you feel now

2. Overall, how would you say you feel now compared to how you felt when you first contacted us?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| I feel a lot worse | I feel slightly worse | I feel neither better nor worse | I feel somewhat better | I feel a lot better |

**Other treatment**

2. During the last 4 months have you had any other treatment for depression apart from seeing the primary care worker? Tick all that apply:

☐ Prescribed medication

- ☐ Referral for talking therapy – eg counsellor, psychologist
- ☐ Advice from your GP
- ☐ Psychiatric assessment
- ☐ Other: _____

3. If referred on to somewhere else, did you attend appointments?

Yes☐ No ☐ Does not apply☐

**Medication**

4. If you have been prescribed antidepressant medication, please answer the following:

| | Yes | No |
|---|---|---|
| Do you ever forget to take your antidepressants? | ☐ | ☐ |
| Are you careless at times about taking your antidepressants? | ☐ | ☐ |
| When you feel better, do you sometimes stop taking your antidepressants? | ☐ | ☐ |
| Sometimes when you feel worse, do you stop taking your antidepressants? | ☐ | ☐ |

**Self Help**

5. If you were given any booklets, how much of them have you read?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| Nothing | Less than half | Half | More than half | All the booklet/s |

6. If you used the self-help booklets, how easy were they to use?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| Extremely easy | Quite easy | Neutral | Not very easy | Hard to use |

7. Please rate each booklet that you read:

| | **Extremely helpful** | | | | **Not at all helpful** |
|---|---|---|---|---|---|
| "Antidepressants" | 1 | 2 | 3 | 4 | 5 |
| "Depression and Low mood" | 1 | 2 | 3 | 4 | 5 |
| "Stress and Anxiety" | 1 | 2 | 3 | 4 | 5 |
| "Panic" | 1 | 2 | 3 | 4 | 5 |
| Other Self-help material | 1 | 2 | 3 | 4 | 5 |

8. Are you using any of the exercises recommended by the booklets?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |
| Not at all | Occasionally | Quite Often | Frequently | Very frequently |

**The Primary Care Worker**

9. How helpful did you find your contact with the primary care worker?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| Extremely unhelpful | Rather unhelpful | Neither helpful nor unhelpful | Somewhat helpful | Extremely helpful |

10. To what extent did you feel that the primary care worker understood your problems?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| Very much so | Moderately | Neutral | Not really | Not at all |

11. Would the self help materials have been as helpful without the support of the primary care worker?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| Definitely not | Probably not | Not sure | Probably | Definitely yes |

12. What do you think about the number of times you had contact with the primary care worker (including both face to face and telephone contacts)?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| I would have preferred more contacts | | I was happy with the number of contacts | | I thought that there were too many contacts |

13. What do you think about the length of each meeting with the primary care worker?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| They were too short | | They were long enough to be helpful | | They were too long |

14. Some of your contacts might have been over the phone. How helpful you did you find this?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| Extremely unhelpful | Rather unhelpful | Neither helpful nor unhelpful | Somewhat helpful | Extremely helpful |

## Future Management of Problems

15. If you became depressed again, do you now think you would cope better with it?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| Definitely not | Probably not | Not sure | Probably yes | Definitely yes |

### ***The Service Generally***

16. If you have had previous treatment for depression, how did this service compare?

| ☐ | ☐ | ☐ | ☐ | ☐ |
|---|---|---|---|---|
| It was definitely not as good | It was not quite as good | It was about the same/not sure | It was a little better | It was much better |

**Your reasons for seeking help and your comments on the services**

*This section contains questions about services you have received. The services you have received means all the help you have had. This might include advice from your GP, anti-depressants, meeting with the primary care worker or counselling.*

17. Why did you decide to ask for help with your depression on this occasion?

_____

_____

_____

_____

18. What problems were you hoping would be helped by the services you received?

_____

_____

_____

_____

_____

19. Which parts of the services did you find most helpful, and can you say why?

_____

_____

_____

_____

20. Have the services you received helped you have a better understanding of why you became depressed?

21. Do you think the services could be changed in any way, to make them more helpful?

22. If you did not complete any of the services you were offered (including anti-depressants, counselling etc.), could you give your reasons?

23. Do you have any other comments about the services?

## Appendix R Focus Group Questions

1. What has been the practices overall experience of the enhanced care study? (Positives, negatives, problems)

2. Do you think that the requirements of the research had any impact on the ability of you or the PCMHW's to provide the service? (e.g. randomisation)

3. Flyers were sent out as part of the project recruitment
   Do you think that they were useful?
   Did they create any problems?
   Did patients like them?

4. Searches on EMIS were used to find suitable patient what views do you have on this?
   How well did it work?
   Were there any difficulties?

5. Was your workload/caseload affected in any way by the project and if so how?

5. Did the project help with the identification or treatment of depression in this practice?

6. Do you think that any changes arising from the project will continue after the project has finished?
   Did it have any impact on practice systems/support staff structures?
   Will they be sustained?

7. What is your view of the enhanced care service offered by the PCMHW's
   Is it a feasible role for them to take on?
   What was most useful?
   What could be improved?
   Could someone else in the practice take on this role?
   Might it be used with other groups than depressed patients or just limited?

8. Did you get any feedback from patients regarding the enhanced care intervention?

9. Would you support offering ECD as part of the role of PCMHW's in practices across the PCT?

10. Any other comments